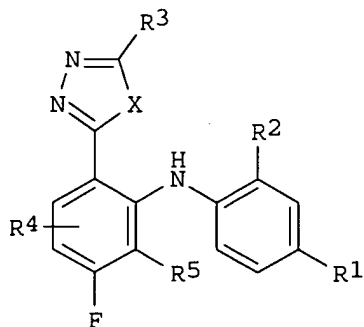


=> d ibib abs hitstr 123 1-17

L23 ANSWER 1 OF 17 HCAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2004:546489 HCAPLUS
 DOCUMENT NUMBER: 141:106474
 TITLE: Preparation of MEK **inhibiting** oxa- and
 thiadiazol-2-ylphenylamines
 INVENTOR(S): Biwersi, Cathlin Marie; Warmus, Joseph Scott; Zhang,
 Lu Yan; Barrett, Stephen Douglas; Kaufman, Michael
 David; Plummer, Mark Stephen; **Reed, Jessica
 Elizabeth**
 PATENT ASSIGNEE(S): Warner-Lambert Company Llc, USA
 SOURCE: PCT Int. Appl., 130 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|-------------------|-----------------|------------|
| WO 2004056789 | A1 | 20040708 | WO 2003-IB5787 | 20031208 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2005004186 | A1 | 20050106 | US 2003-725206 | 20031201 |
| PRIORITY APPLN. INFO.: | | | US 2002-435155P | P 20021220 |
| | | | US 2003-509701P | P 20031008 |
| OTHER SOURCE(S): | | MARPAT 141:106474 | | |
| GI | | | | |



I

AB Title compds. I [X = Nh, O, S; R1 = (un)substituted alkyl, alkenyl,
 C.tplbond.CH, alkoxy, acyl, CONH2, CO2H, alkylthio; R2 = F, CH2F, CHF2,
 CF3; R3 = (un)substituted alkyl, alkenyl, aryl, OH, SH; R4 = H, halogen;
 R5 = H, F] were prepared for use as **inhibitors** of MAPKIERK
Kinase (MEK) enzymes in immunomodulation and in the treatment and

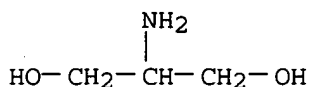
alleviation of inflammation, and proliferative diseases such as cancer and restenosis (no data). Thus, 2-(4-bromo-2-fluorophenylamino)-3,4-difluorobenzoic acid was converted to its hydrazide and cyclized with BrCN to give I [X = O, R1 = Br, R2, R5 = F, R3 = NH2, R4 = H].

IT 534-03-2, 2-Amino-1,3-propanediol 61278-21-5,
(S)-(-)-3-Amino-1,2-propanediol 66211-46-9, (2R)-3-Amino-1,2-propanediol

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of MEK **inhibiting** oxa- and thiadiazol-2-ylphenylamines)

RN 534-03-2 HCAPLUS

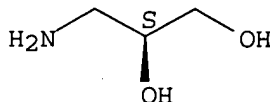
CN 1,3-Propanediol, 2-amino- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 61278-21-5 HCAPLUS

CN 1,2-Propanediol, 3-amino-, (2S)- (9CI) (CA INDEX NAME)

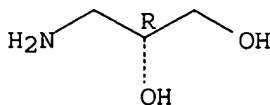
Absolute stereochemistry. Rotation (-).



RN 66211-46-9 HCAPLUS

CN 1,2-Propanediol, 3-amino-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 2 OF 17 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:80385 HCAPLUS

DOCUMENT NUMBER: 140:146153

TITLE: Preparation of pyrimidopyrimidinones as **kinase inhibitors**

INVENTOR(S): Chivikas, Connolly Cleo J.; **Deur, Christopher James; Hamby, James Marino; Hoyer, Denton Wade; Limberakis, Chris; Reed, Jessica Elizabeth; Schroeder, Mel Conrad; Taylor, Clarke**

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 44 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

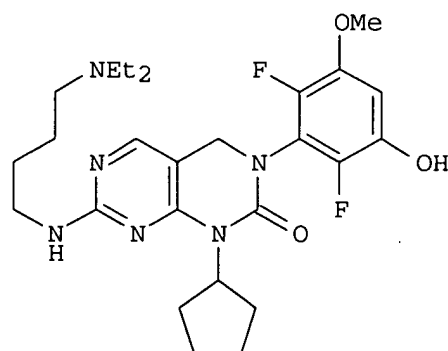
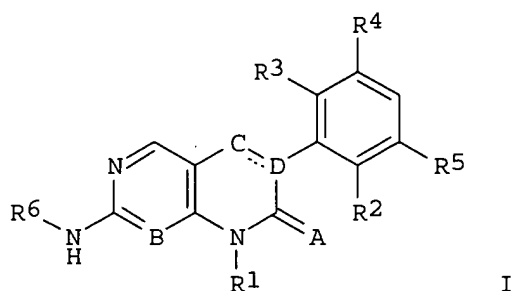
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| US 2004019210 | A1 | 20040129 | US 2003-621983 | 20030717 |
| CA 2493633 | AA | 20040205 | CA 2003-2493633 | 20030721 |
| WO 2004011465 | A1 | 20040205 | WO 2003-IB3359 | 20030721 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRIORITY APPLN. INFO.: | | | US 2002-398638P | P 20020725 |
| | | | WO 2003-IB3359 | W 20030721 |

OTHER SOURCE(S): MARPAT 140:146153
GI



AB This invention provides phenyl-substituted pyrimidopyrimidines, dihydropyrimidopyrimidines, pyridopyrimidines, naphthyridines, and pyridopyrazines of the general formula I [A = O, NH₂, mono(or di)alkylamino, NHCONHR₁₂ (wherein R₁₂ = alkyl, alkylencycloalkyl); B, C, D = CH, N (with the proviso that C and D are not both N); R₁ = alkyl

(optionally substituted by CO₂H), (un)substituted Ph, CH₂Ph, piperidiny1, etc.; R₂ = H, Cl, F; R₃ = H, Cl, F (at least one of R₂ or R₃ = F); R₄ = H, OH, OMe, OEt (if R₄ = H, R₂ and R₃ is not H); R₅ = OMe, OEt; R₆ = H, alkyl-NH₂, O-alkyl-NH₂, etc.] that **inhibit** cyclin-dependent **kinase** and tyrosine **kinase** enzymes, methods and intermediates for their synthesis, as well as pharmaceutical compns. and methods for their use in treating, **inhibiting** or preventing maladies associated with cell proliferative disorders, including angiogenesis, atherosclerosis, restenosis, and cancer (no biol. data given). Synthesis of 35 title compds. I is described. E.g., a multi-step synthesis of II was given.

IT 62031-54-3, Fibroblast growth factor 62229-50-9,
Epidermal growth factor 141349-86-2, Cdk2 **kinase**
143375-65-9, Cdc2 **kinase** 144697-17-6, c-Src
kinase 147014-97-9, Cdk4 **kinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of pyrimidopyrimidinones as **kinase inhibitors**
)

RN 62031-54-3 HCAPLUS
CN Fibroblast growth factor (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 62229-50-9 HCAPLUS
CN Epidermal growth factor (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 141349-86-2 HCAPLUS
CN Kinase (phosphorylating), gene cdk2 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 143375-65-9 HCAPLUS
CN Kinase (phosphorylating), gene cdc2 protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 144697-17-6 HCAPLUS
CN Kinase (phosphorylating), gene c-src protein (9CI) (CA INDEX NAME)

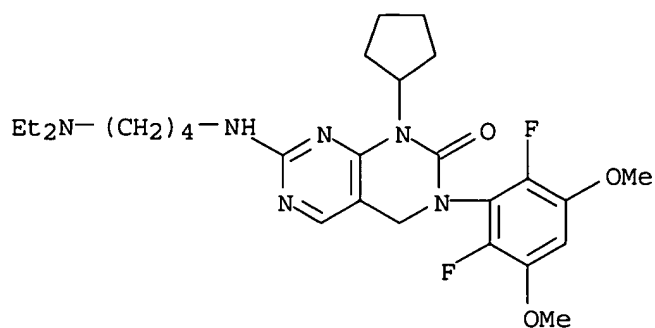
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 147014-97-9 HCAPLUS
CN Kinase (phosphorylating), protein p33CDK4 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 651734-15-5P 651734-16-6P 651734-35-9P
651734-43-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyrimidopyrimidinones as **kinase inhibitors**
)

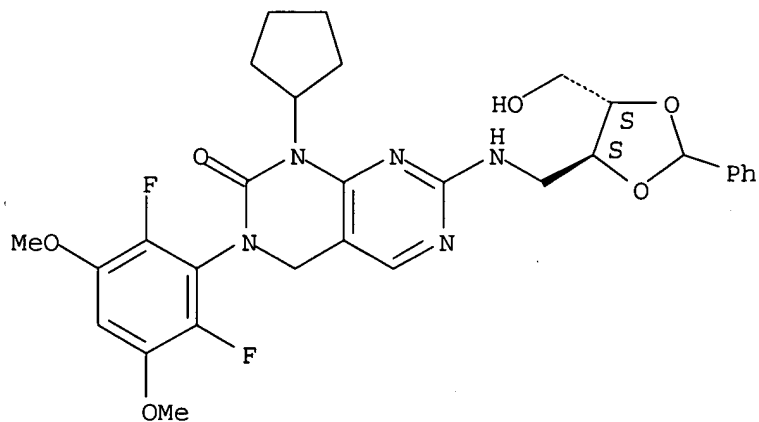
RN 651734-15-5 HCAPLUS
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-7-[[4-
(diethylamino)butyl]amino]-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-
dihydro- (9CI) (CA INDEX NAME)



RN 651734-16-6 HCAPLUS

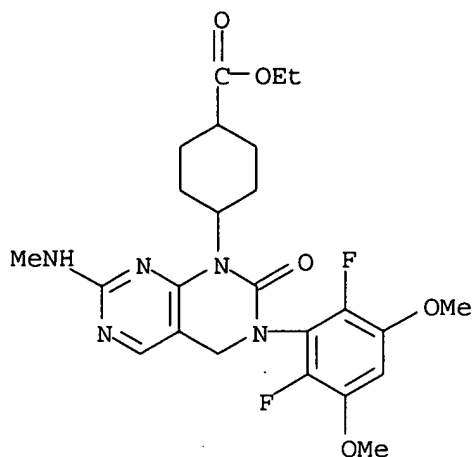
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[[[(4S,5S)-5-(hydroxymethyl)-2-phenyl-1,3-dioxolan-4-yl]methyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



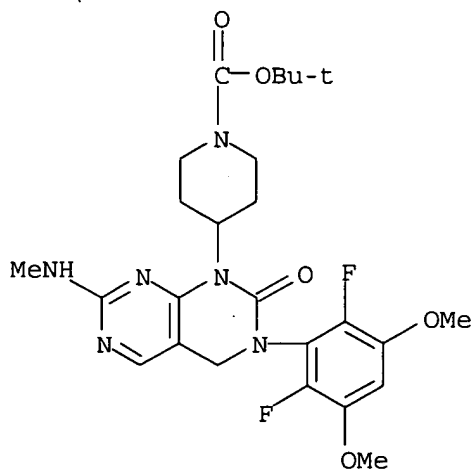
RN 651734-35-9 HCAPLUS

CN Cyclohexanecarboxylic acid, 4-[3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 651734-43-9 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



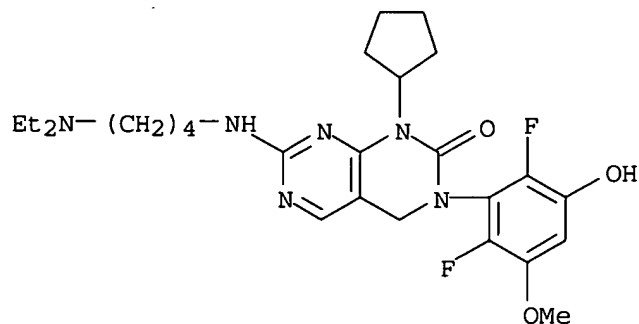
IT 651734-14-4P 651734-17-7P 651734-18-8P
 651734-19-9P 651734-20-2P 651734-21-3P
 651734-22-4P 651734-23-5P 651734-24-6P
 651734-25-7P 651734-26-8P 651734-27-9P
 651734-28-0P 651734-29-1P 651734-30-4P
 651734-31-5P 651734-32-6P 651734-33-7P
 651734-34-8P 651734-36-0P 651734-38-2P
 651734-39-3P 651734-40-6P 651734-41-7P
 651734-42-8P 651734-45-1P 651734-46-2P
 651734-47-3P 651734-48-4P 651734-49-5P
 651734-50-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrimidopyrimidinones as **kinase inhibitors**)

RN 651734-14-4 HCAPLUS

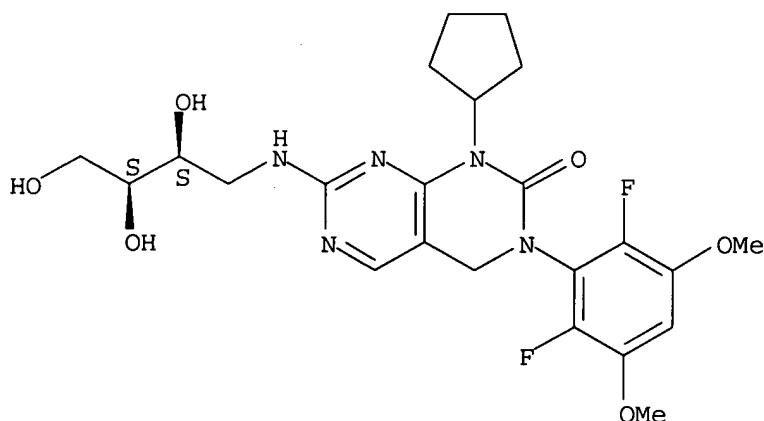
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-7-[[4-(diethylamino)butyl]amino]-3-(2,6-difluoro-3-hydroxy-5-methoxyphenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 651734-17-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[[[(2S,3S)-2,3,4-trihydroxybutyl]amino]- (9CI) (CA INDEX NAME)

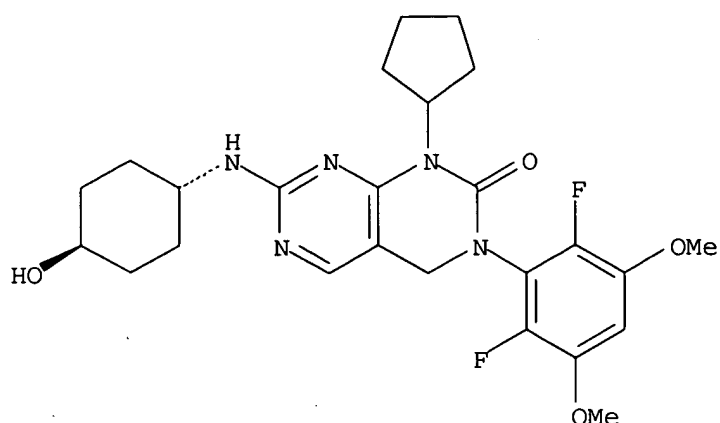
Absolute stereochemistry.



RN 651734-18-8 HCAPLUS

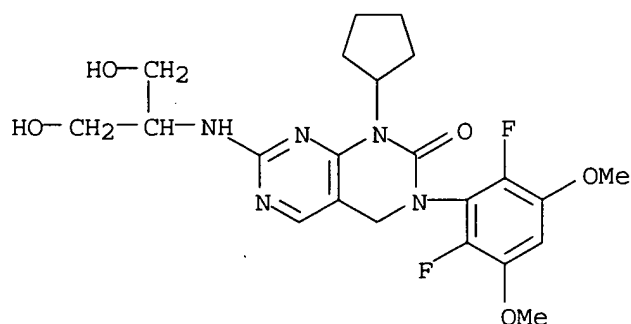
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



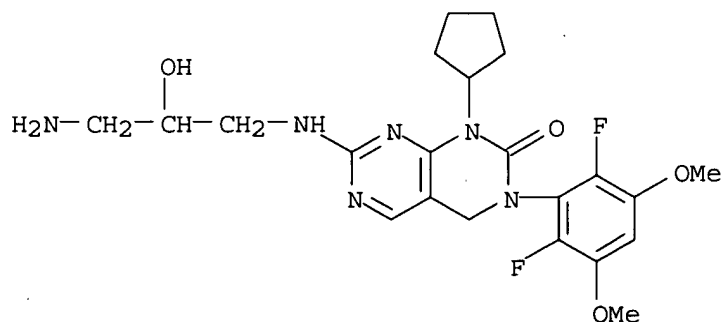
RN 651734-19-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]-(9CI) (CA INDEX NAME)



RN 651734-20-2 HCAPLUS

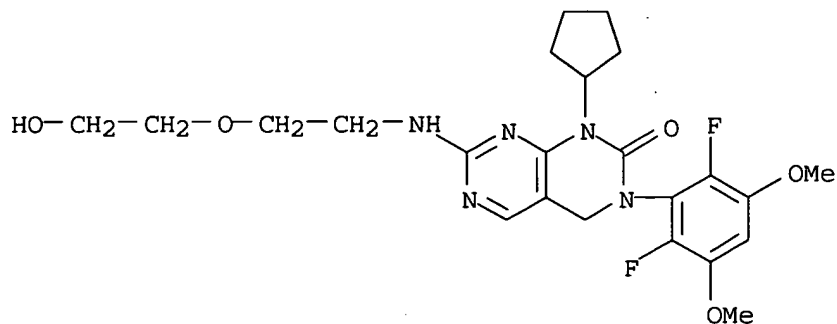
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(3-amino-2-hydroxypropyl)amino]-1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-(9CI) (CA INDEX NAME)



RN 651734-21-3 HCAPLUS

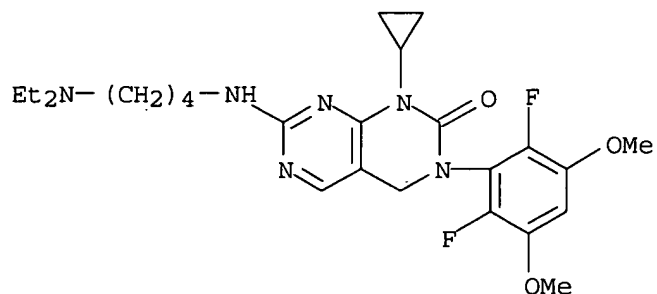
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[[2-(2-hydroxyethoxy)ethyl]amino]-(9CI)

(CA INDEX NAME)



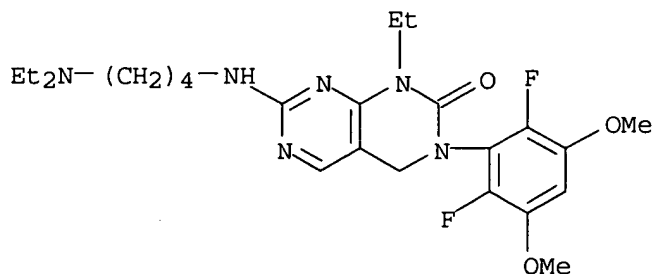
RN 651734-22-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopropyl-7-[[4-(diethylamino)butyl]amino]-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)



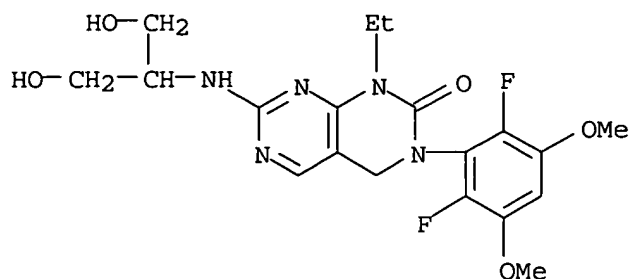
RN 651734-23-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[4-(diethylamino)butyl]amino]-3-(2,6-difluoro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 651734-24-6 HCAPLUS

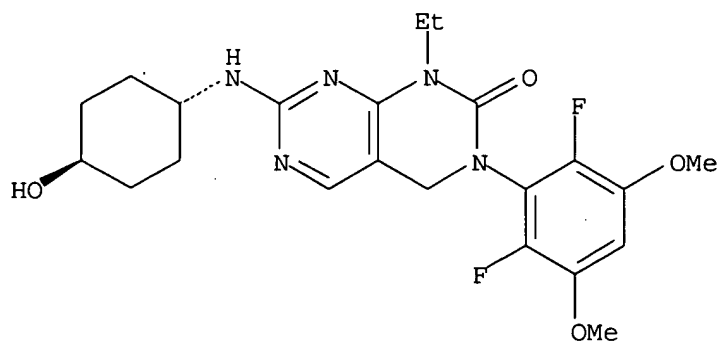
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-difluoro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro-7-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]- (9CI) (CA INDEX NAME)



RN 651734-25-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-difluoro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]- (9CI) (CA INDEX NAME)

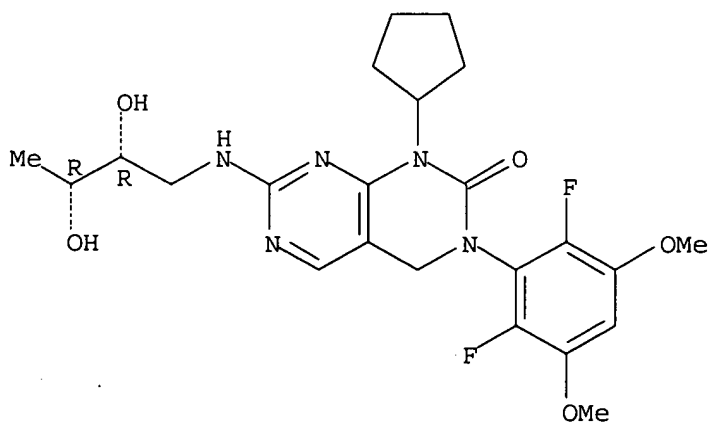
Relative stereochemistry.



RN 651734-26-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-7-[[[(2R,3R)-2,3-dihydroxybutyl]amino]-3,4-dihydro- (9CI) (CA INDEX NAME)

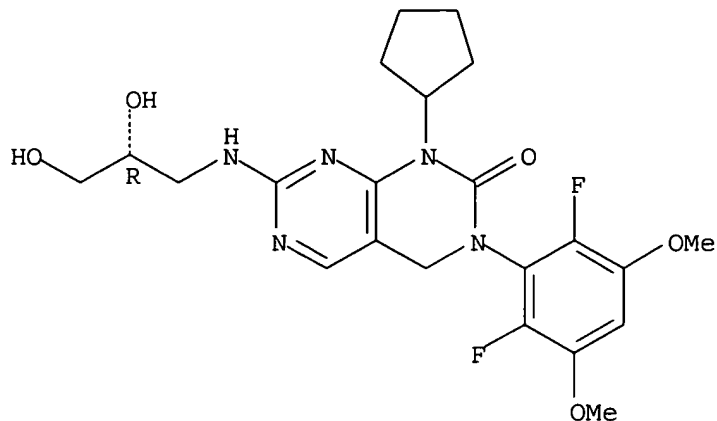
Absolute stereochemistry.



RN 651734-27-9 HCAPLUS

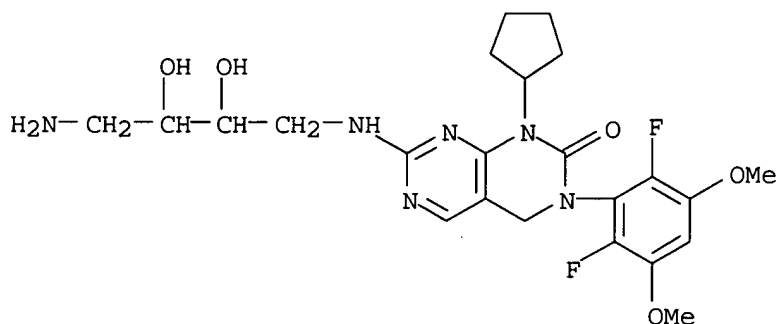
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-7-[[(2R)-2,3-dihydroxypropyl]amino]-3,4-dihydro- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 651734-28-0 HCAPLUS

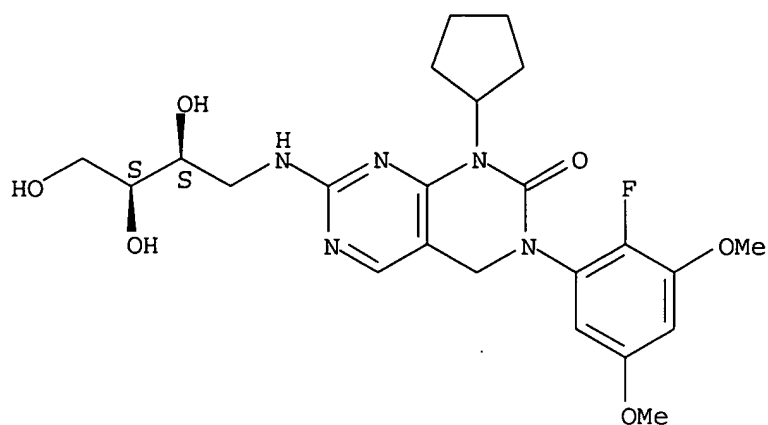
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(4-amino-2,3-dihydroxybutyl)amino]-1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 651734-29-1 HCAPLUS

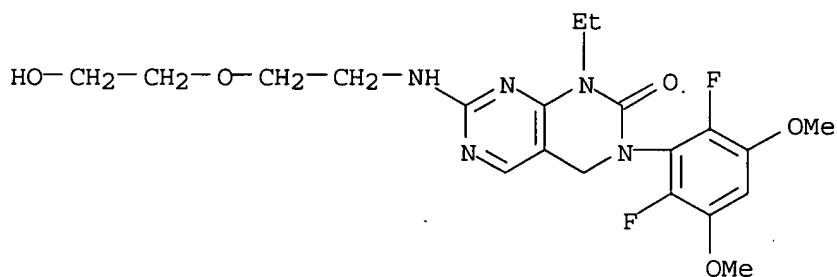
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2-fluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[[(2S,3S)-2,3,4-trihydroxybutyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 651734-30-4 HCAPLUS

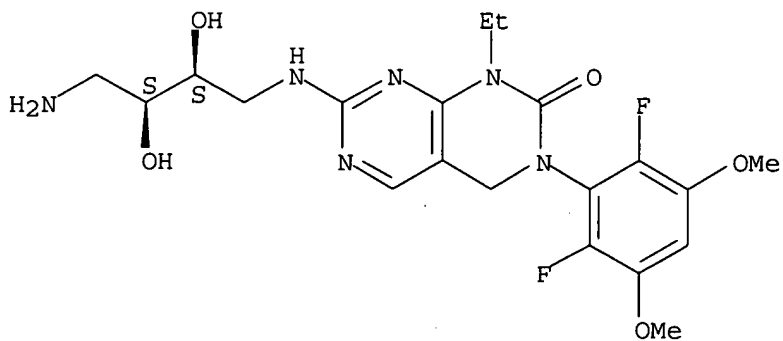
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-difluoro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro-7-[[2-(2-hydroxyethoxy)ethyl]amino] - (9CI) (CA INDEX NAME)



RN 651734-31-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[[(2S,3S)-4-amino-2,3-dihydroxybutyl]amino]-3-(2,6-difluoro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)

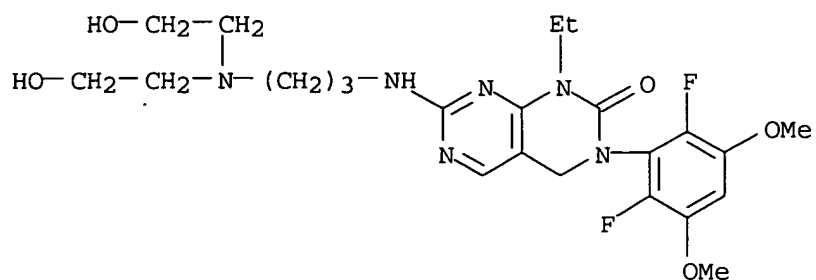
Absolute stereochemistry.



RN 651734-32-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[3-[bis(2-

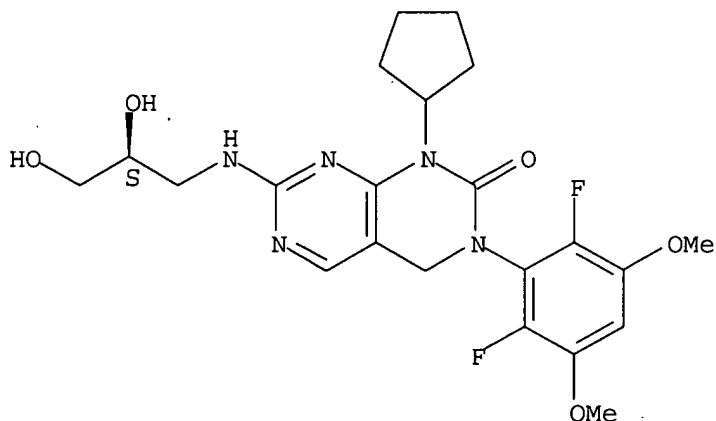
hydroxyethyl)amino]propyl]amino]-3-(2,6-difluoro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 651734-33-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-7-[[(2S)-2,3-dihydroxypropyl]amino]-3,4-dihydro- (9CI) (CA INDEX NAME)

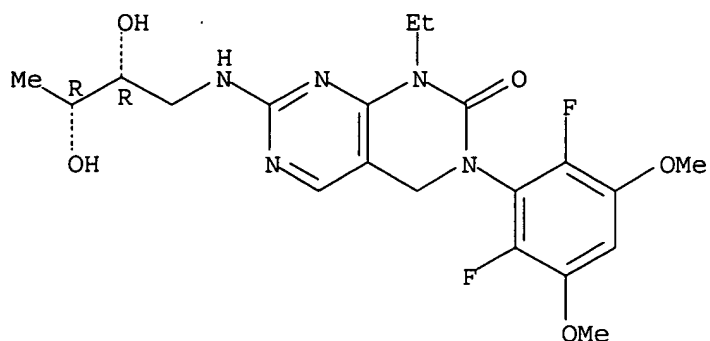
Absolute stereochemistry.



RN 651734-34-8 HCAPLUS

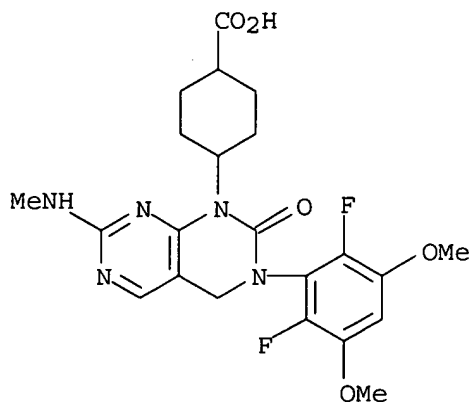
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-difluoro-3,5-dimethoxyphenyl)-7-[[(2R,3R)-2,3-dihydroxybutyl]amino]-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 651734-36-0 HCAPLUS

CN Cyclohexanecarboxylic acid, 4-[3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]- (9CI)
(CA INDEX NAME)



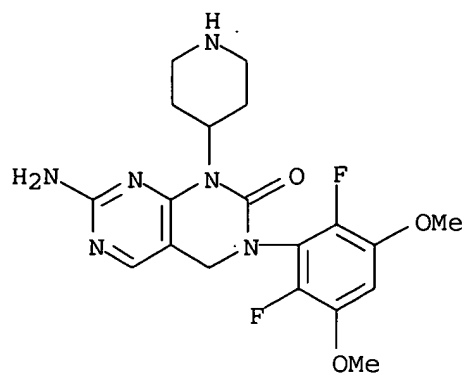
RN 651734-38-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-amino-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-1-(4-piperidinyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 651734-37-1

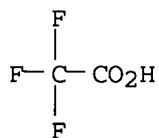
CMF C19 H22 F2 N6 O3



CM 2

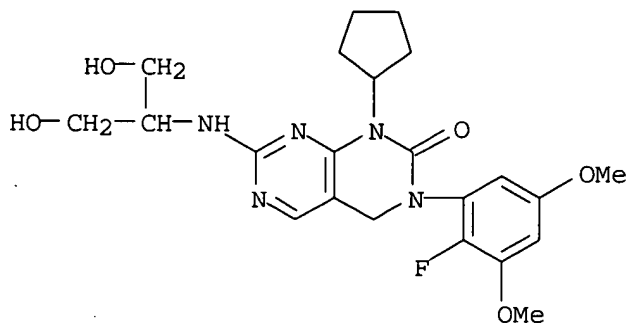
CRN 76-05-1

CMF C2 H F3 O2



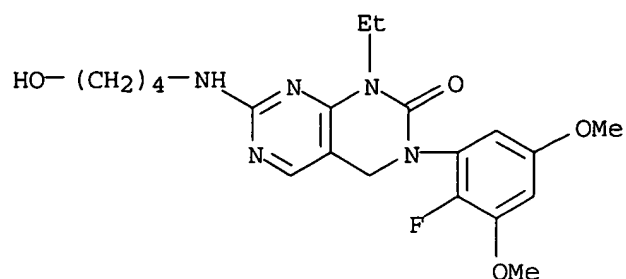
RN 651734-39-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2-fluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]-(9CI) (CA INDEX NAME)



RN 651734-40-6 HCAPLUS

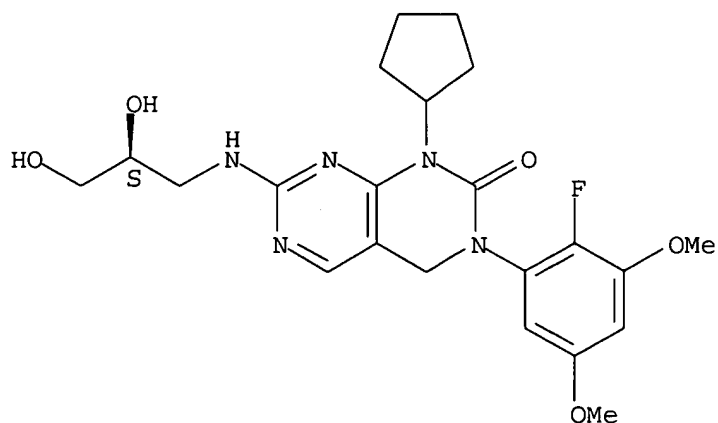
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-ethyl-3-(2-fluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[(4-hydroxybutyl)amino]-(9CI) (CA INDEX NAME)



RN 651734-41-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-7-[(2S)-2,3-dihydroxypropyl]amino]-3-(2-fluoro-3,5-dimethoxyphenyl)-3,4-dihydro- (9CI)
(CA INDEX NAME)

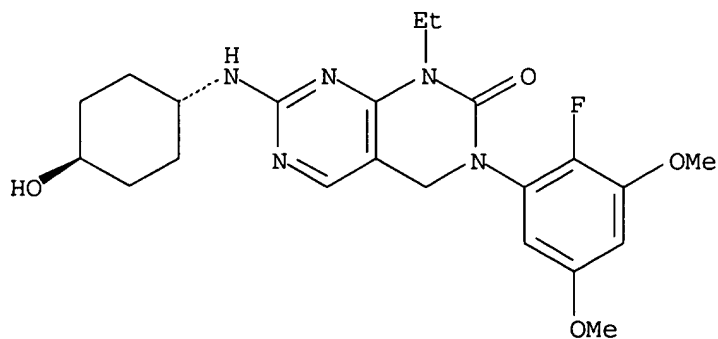
Absolute stereochemistry.



RN 651734-42-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-fluoro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



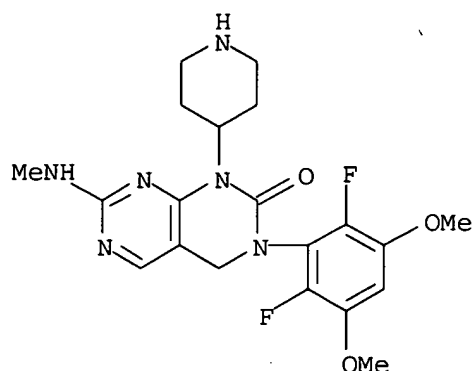
RN 651734-45-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylamino)-1-(4-piperidiny)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 651734-44-0

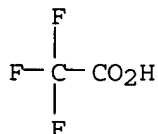
CMF C20 H24 F2 N6 O3



CM 2

CRN 76-05-1

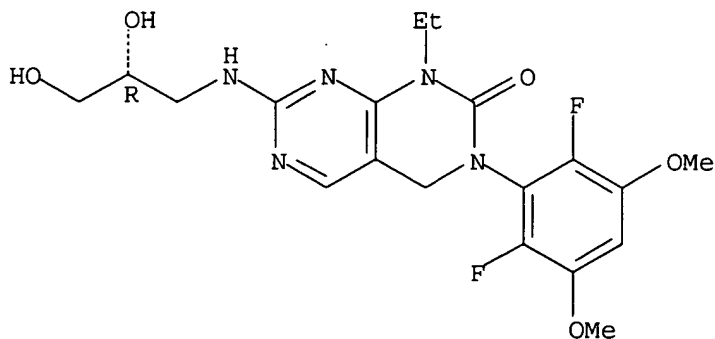
CMF C2 H F3 O2



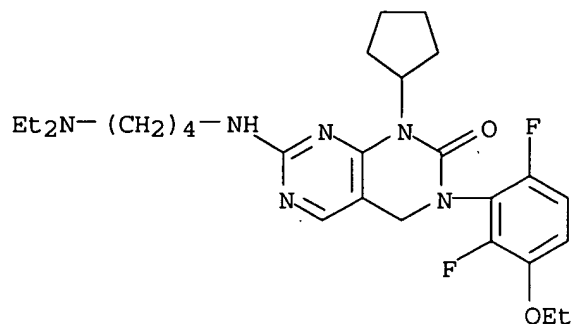
RN 651734-46-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-difluoro-3,5-dimethoxyphenyl)-7-[[(2R)-2,3-dihydroxypropyl]amino]-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

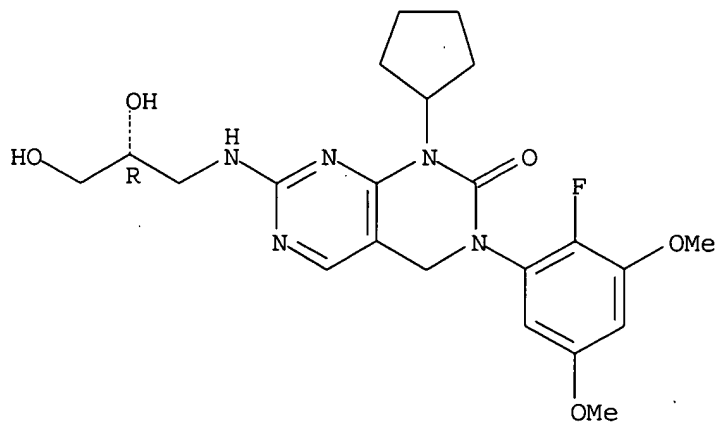


RN 651734-47-3 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-7-[[4-(diethylamino)butyl]amino]-3-(3-ethoxy-2,6-difluorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

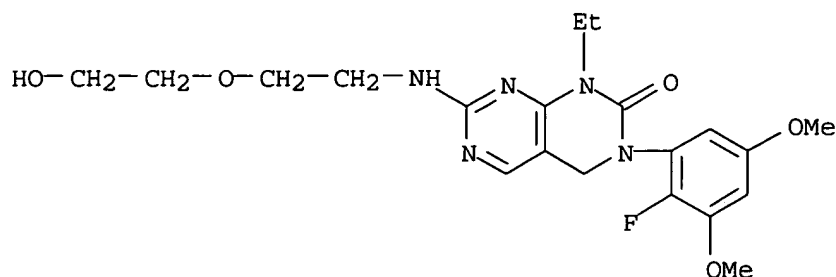


RN 651734-48-4 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-7-[[(2R)-2,3-dihydroxypropyl]amino]-3-(2-fluoro-3,5-dimethoxyphenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



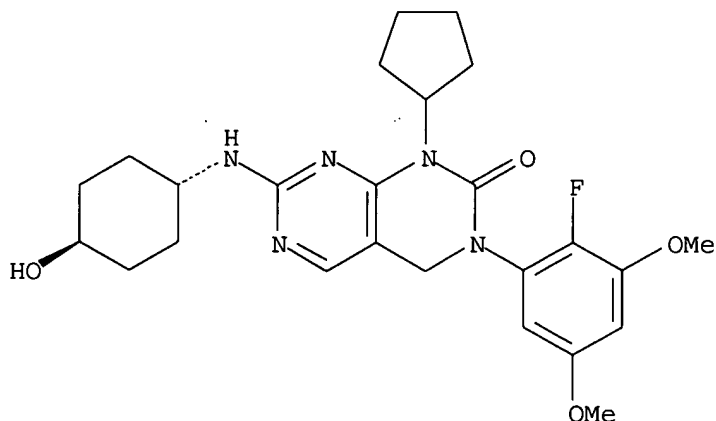
RN 651734-49-5 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-ethyl-3-(2-fluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[[2-(2-hydroxyethoxy)ethyl]amino]- (9CI) (CA INDEX NAME)



RN 651734-50-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2-fluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]- (9CI)
(CA INDEX NAME)

Relative stereochemistry.

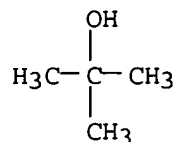


IT 75-65-0, t-Butanol, reactions 100-46-9, Benzylamine, reactions 367-27-1, 2,4-Difluorophenol 534-03-2, Serinol 616-29-5, 1,3-Diamino-2-hydroxypropane 765-30-0, Cyclopropylamine 770-31-0 929-06-6, 2-(2-Aminoethoxy)ethanol 2150-37-0, Methyl 3,5-dimethoxy benzoate 4985-85-7, N-(3-Aminopropyl)diethanolamine 5909-24-0, 4-Chloro-2-methylsulfanylpurimidine-5-carboxylic acid ethyl ester 13325-10-5, 4-Aminobutan-1-ol 17159-80-7, Ethyl-4-hydroxycyclohexanecarboxylate 27431-62-5, 4-Diethylaminobutylamine 27489-62-9, trans-4-Aminocyclohexanol 32798-38-2, 1,4-Diaminobutane-2,3-diol 36629-42-2, Methyl pentafluorobenzoate 61278-21-5 66211-46-9 104769-25-7, (2S,3S)-1,4-Diaminobutane-2,3-diol 109384-19-2, tert-Butyl-4-hydroxy-1-piperidinecarboxylate 155322-89-7, (4S,5R)-2,2,5-Trimethyl[1,3]dioxolane-4-carbonyl chloride 168113-19-7 185040-35-1 211245-64-6 651734-99-5, 1-Cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-7-methylsulfinyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one 651735-01-2 651735-16-9 651735-17-0 651735-19-2

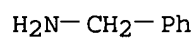
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of pyrimidopyrimidinones as **kinase inhibitors**)

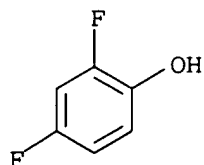
)
 RN 75-65-0 HCAPLUS
 CN 2-Propanol, 2-methyl- (9CI) (CA INDEX NAME)



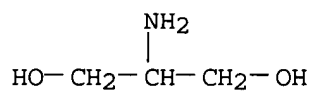
RN 100-46-9 HCAPLUS
 CN Benzenemethanamine (9CI) (CA INDEX NAME)



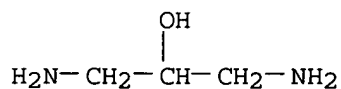
RN 367-27-1 HCAPLUS
 CN Phenol, 2,4-difluoro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



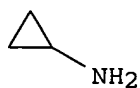
RN 534-03-2 HCAPLUS
 CN 1,3-Propanediol, 2-amino- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 616-29-5 HCAPLUS
 CN 2-Propanol, 1,3-diamino- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

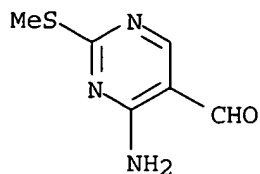


RN 765-30-0 HCAPLUS
 CN Cyclopropanamine (9CI)• (CA INDEX NAME)



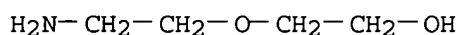
RN 770-31-0 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI)
(CA INDEX NAME)



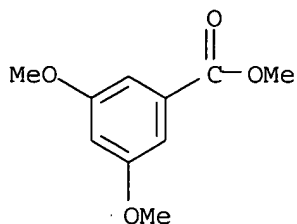
RN 929-06-6 HCAPLUS

CN Ethanol, 2-(2-aminoethoxy)- (7CI, 8CI, 9CI) (CA INDEX NAME)



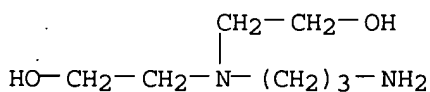
RN 2150-37-0 HCAPLUS

CN Benzoic acid, 3,5-dimethoxy-, methyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



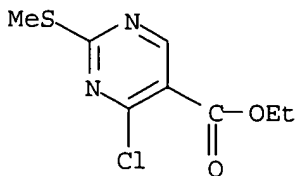
RN 4985-85-7 HCAPLUS

CN Ethanol, 2,2'-[(3-aminopropyl)imino]bis- (9CI) (CA INDEX NAME)



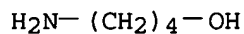
RN 5909-24-0 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-chloro-2-(methylthio)-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



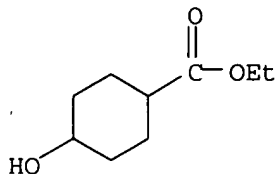
RN 13325-10-5 HCAPLUS

CN 1-Butanol, 4-amino- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



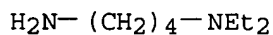
RN 17159-80-7 HCAPLUS

CN Cyclohexanecarboxylic acid, 4-hydroxy-, ethyl ester (6CI, 7CI, 8CI, 9CI)
(CA INDEX NAME)



RN 27431-62-5 HCAPLUS

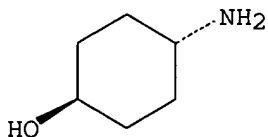
CN 1,4-Butanediamine, N,N-diethyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 27489-62-9 HCAPLUS

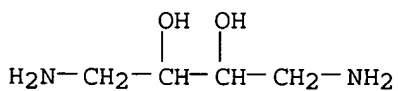
CN Cyclohexanol, 4-amino-, trans- (8CI, 9CI) (CA INDEX NAME)

Relative stereochemistry.



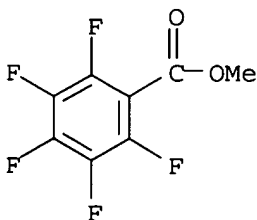
RN 32798-38-2 HCAPLUS

CN 2,3-Butanediol, 1,4-diamino- (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 36629-42-2 HCAPLUS

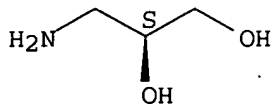
CN Benzoic acid, pentafluoro-, methyl ester (9CI) (CA INDEX NAME)



RN 61278-21-5 HCAPLUS

CN 1,2-Propanediol, 3-amino-, (2S)- (9CI) (CA INDEX NAME)

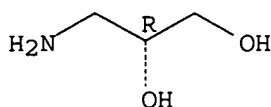
Absolute stereochemistry. Rotation (-).



RN 66211-46-9 HCAPLUS

CN 1,2-Propanediol, 3-amino-, (2R)- (9CI) (CA INDEX NAME)

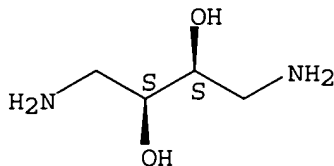
Absolute stereochemistry. Rotation (+).



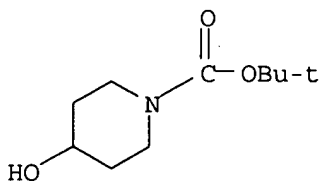
RN 104769-25-7 HCAPLUS

CN 2,3-Butanediol, 1,4-diamino-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



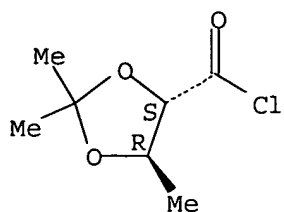
RN 109384-19-2 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-hydroxy-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)

RN 155322-89-7 HCAPLUS

CN 1,3-Dioxolane-4-carbonyl chloride, 2,2,5-trimethyl-, (4S,5R)- (9CI) (CA INDEX NAME)

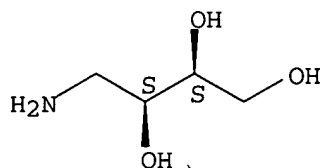
Absolute stereochemistry.



RN 168113-19-7 HCAPLUS

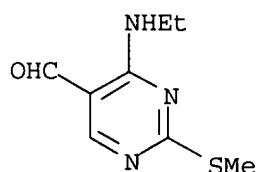
CN 1,2,3-Butanetriol, 4-amino-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



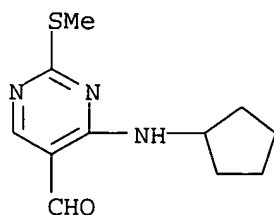
RN 185040-35-1 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



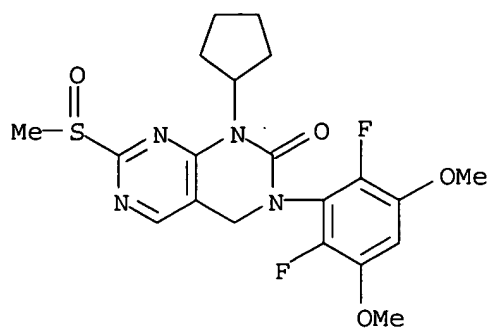
RN 211245-64-6 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-(cyclopentylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



RN 651734-99-5 HCAPLUS

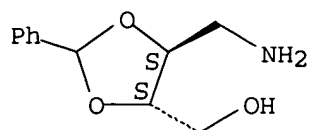
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylsulfinyl)- (9CI) (CA INDEX NAME)



RN 651735-01-2 HCAPLUS

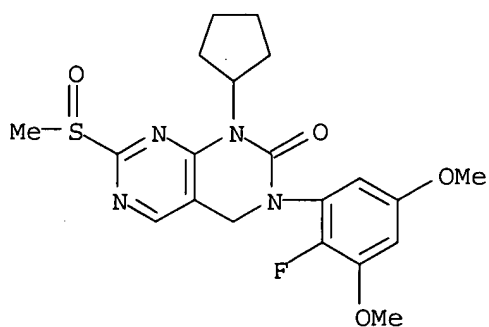
CN 1,3-Dioxolane-4-methanol, 5-(aminomethyl)-2-phenyl-, (4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



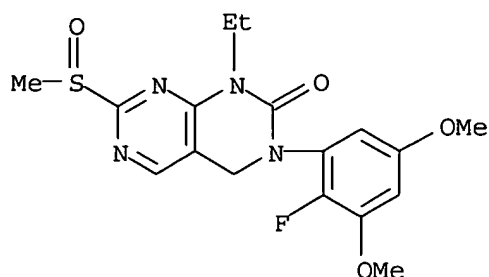
RN 651735-16-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2-fluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylsulfinyl)- (9CI) (CA INDEX NAME)

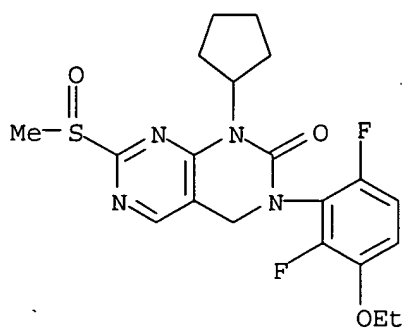


RN 651735-17-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-ethyl-3-(2-fluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylsulfinyl)- (9CI) (CA INDEX NAME)



RN 651735-19-2 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(3-ethoxy-2,6-difluorophenyl)-3,4-dihydro-7-(methylsulfinyl)- (9CI) (CA INDEX NAME)



IT 348-20-9P, 1-Ethoxy-2,4-difluorobenzene 122590-82-3P,
 Methyl 4-(benzylamino)-2,3,5,6-tetrafluorobenzoate 211247-46-0P
 651734-51-9P, Methyl 4-(benzylamino)-3,5-difluoro-2,6-
 dimethoxybenzoate 651734-52-0P, 4-(Benzylamino)-3,5-difluoro-2,6-
 dimethoxybenzoic Acid 651734-53-1P, N-Benzyl-2,6-difluoro-3,5-
 dimethoxyaniline 651734-54-2P, 2,6-Difluoro-3,5-dimethoxyaniline
 651734-55-3P, 2,6-Difluoro-3,5-dimethoxybenzoic acid Methyl Ester
 651734-56-4P, 2,6-Difluoro-3,5-dimethoxybenzoic acid
 651734-57-5P, (2,6-Difluoro-3,5-dimethoxyphenyl)carbamic acid
 tert-Butyl Ester 651734-58-6P, 2-Fluoro-3,5-dimethoxybenzoic
 Acid Methyl Ester 651734-59-7P, 2-Fluoro-3,5-dimethoxybenzoic
 acid 651734-60-0P, (2-Fluoro-3,5-dimethoxyphenyl)carbamic Acid
 tert-Butyl Ester 651734-61-1P, 2-Fluoro-3,5-dimethoxyphenylamine
 651734-62-2P, 3-Ethoxy-2,6-difluorobenzoic Acid
 651734-63-3P, (3-Ethoxy-2,6-difluorophenyl)carbamic Acid
 tert-Butyl Ester 651734-64-4P, 3-Ethoxy-2,6-difluorophenylamine
 651734-65-5P, 4-Cyclopropylamino-2-methylsulfanylpurimidine-5-
 Carboxylic Acid Ethyl Ester 651734-66-6P 651734-67-7P
 651734-68-8P 651734-69-9P 651734-70-2P
 651734-71-3P 651734-72-4P 651734-73-5P
 651734-74-6P 651734-75-7P 651734-76-8P,
 1-Cyclopropyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-7-methylsulfanyl-3,4-
 dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one 651734-77-9P,
 1-Cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-7-methylsulfanyl-3,4-
 dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one 651734-79-1P
 651734-81-5P 651734-83-7P 651734-86-0P
 651734-88-2P, (4S,5R)-2,2,5-Trimethyl-[1,3]dioxolane-4-carboxylic
 Acid Benzylamide 651734-90-6P, (2S,3R)-N-Benzyl-2,3-

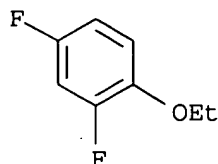
dihydroxybutyramide **651734-92-8P**, (2R,3R)-1-Benzylaminobutane-2,3-diol **651734-94-0P**, (2R,3R)-1-Aminobutane-2,3-diol **651735-06-7P** **651735-08-9P** **651735-10-3P**, 3-(2,6-Difluoro-3,5-dimethoxyphenyl)-7-methylsulfanyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **651735-13-6P** **651735-14-7P** **651735-15-8P** **651735-18-1P** **651735-20-5P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyrimidopyrimidinones as **kinase inhibitors**)

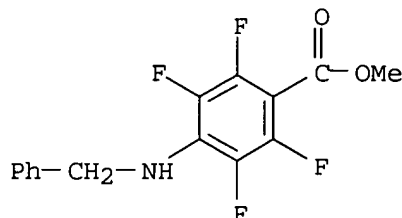
RN 348-20-9 HCAPLUS

CN Benzene, 1-ethoxy-2,4-difluoro- (9CI) (CA INDEX NAME)



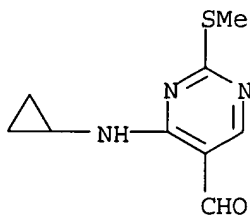
RN 122590-82-3 HCAPLUS

CN Benzoic acid, 2,3,5,6-tetrafluoro-4-[(phenylmethyl)amino]-, methyl ester (9CI) (CA INDEX NAME)



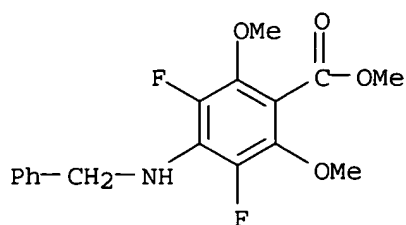
RN 211247-46-0 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-(cyclopropylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)

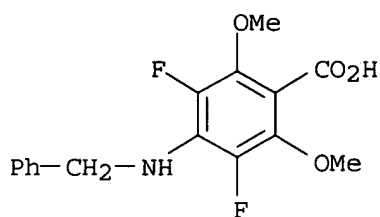


RN 651734-51-9 HCAPLUS

CN Benzoic acid, 3,5-difluoro-2,6-dimethoxy-4-[(phenylmethyl)amino]-, methyl ester (9CI) (CA INDEX NAME)

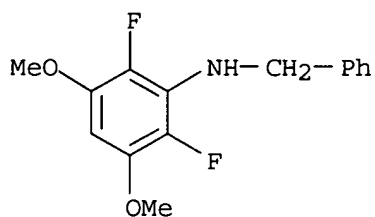


RN 651734-52-0 HCAPLUS

CN Benzoic acid, 3,5-difluoro-2,6-dimethoxy-4-[(phenylmethyl)amino]- (9CI)
(CA INDEX NAME)

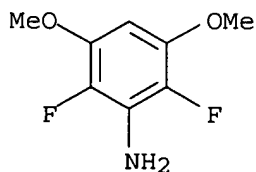
RN 651734-53-1 HCAPLUS

CN Benzenemethanamine, N-(2,6-difluoro-3,5-dimethoxyphenyl)- (9CI) (CA INDEX NAME)



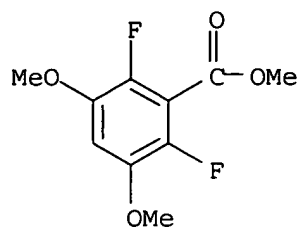
RN 651734-54-2 HCAPLUS

CN Benzenamine, 2,6-difluoro-3,5-dimethoxy- (9CI) (CA INDEX NAME)



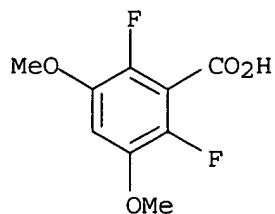
RN 651734-55-3 HCAPLUS

CN Benzoic acid, 2,6-difluoro-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)



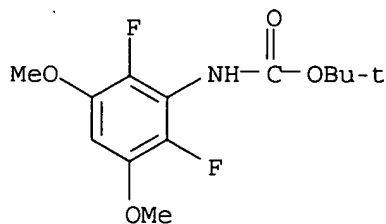
RN 651734-56-4 HCAPLUS

CN Benzoic acid, 2,6-difluoro-3,5-dimethoxy- (9CI) (CA INDEX NAME)



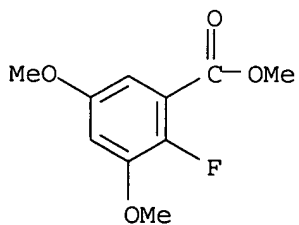
RN 651734-57-5 HCAPLUS

CN Carbamic acid, (2,6-difluoro-3,5-dimethoxyphenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



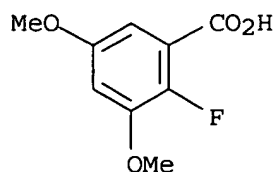
RN 651734-58-6 HCAPLUS

CN Benzoic acid, 2-fluoro-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)



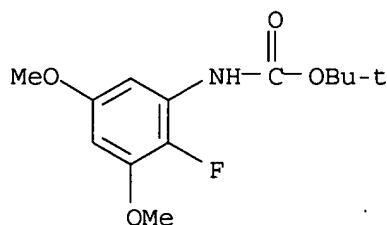
RN 651734-59-7 HCAPLUS

CN Benzoic acid, 2-fluoro-3,5-dimethoxy- (9CI) (CA INDEX NAME)



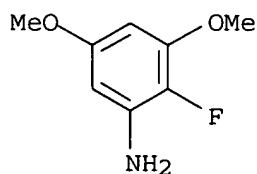
RN 651734-60-0 HCAPLUS

CN Carbamic acid, (2-fluoro-3,5-dimethoxyphenyl)-, 1,1-dimethylethyl ester
(9CI) (CA INDEX NAME)



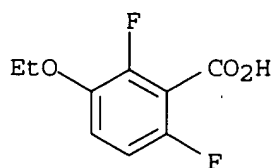
RN 651734-61-1 HCAPLUS

CN Benzenamine, 2-fluoro-3,5-dimethoxy- (9CI) (CA INDEX NAME)



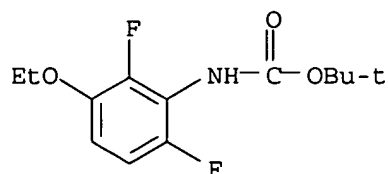
RN 651734-62-2 HCAPLUS

CN Benzoic acid, 3-ethoxy-2,6-difluoro- (9CI) (CA INDEX NAME)



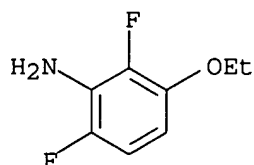
RN 651734-63-3 HCAPLUS

CN Carbamic acid, (3-ethoxy-2,6-difluorophenyl)-, 1,1-dimethylethyl ester
(9CI) (CA INDEX NAME)



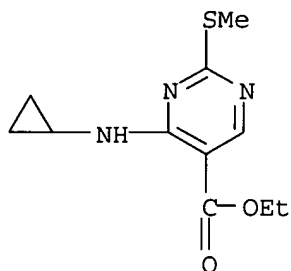
RN 651734-64-4 HCAPLUS

CN Benzenamine, 3-ethoxy-2,6-difluoro- (9CI) (CA INDEX NAME)



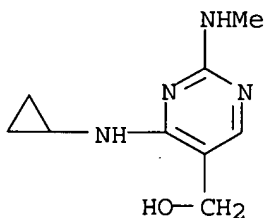
RN 651734-65-5 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-(cyclopropylamino)-2-(methylthio)-, ethyl ester (9CI) (CA INDEX NAME)



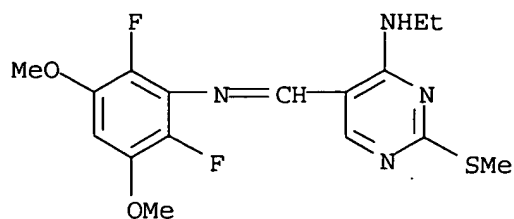
RN 651734-66-6 HCAPLUS

CN 5-Pyrimidinemethanol, 4-(cyclopropylamino)-2-(methylamino)- (9CI) (CA INDEX NAME)



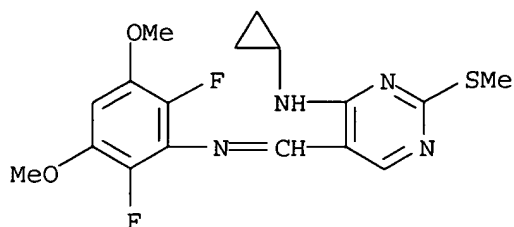
RN 651734-67-7 HCAPLUS

CN 4-Pyrimidinamine, 5-[[[(2,6-difluoro-3,5-dimethoxyphenyl)imino]methyl]-N-ethyl-2-(methylthio)- (9CI) (CA INDEX NAME)



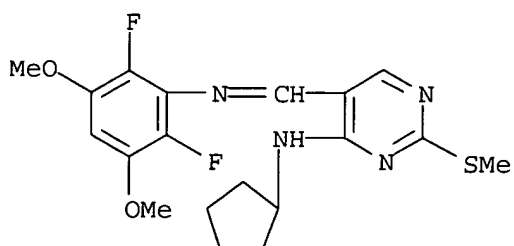
RN 651734-68-8 HCAPLUS

CN 4-Pyrimidinamine, N-cyclopropyl-5-[[2,6-difluoro-3,5-dimethoxyphenyl]imino]methyl]-2-(methylthio)- (9CI) (CA INDEX NAME)



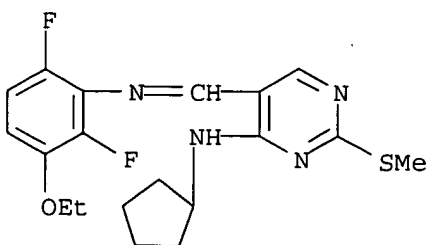
RN 651734-69-9 HCAPLUS

CN 4-Pyrimidinamine, N-cyclopentyl-5-[[2,6-difluoro-3,5-dimethoxyphenyl]imino]methyl]-2-(methylthio)- (9CI) (CA INDEX NAME)



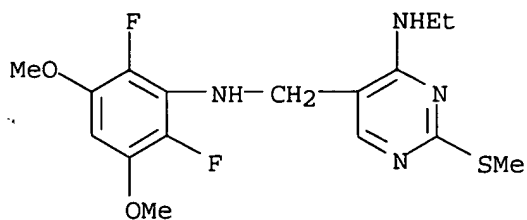
RN 651734-70-2 HCAPLUS

CN 4-Pyrimidinamine, N-cyclopentyl-5-[[3-ethoxy-2,6-difluorophenyl]imino]methyl]-2-(methylthio)- (9CI) (CA INDEX NAME)



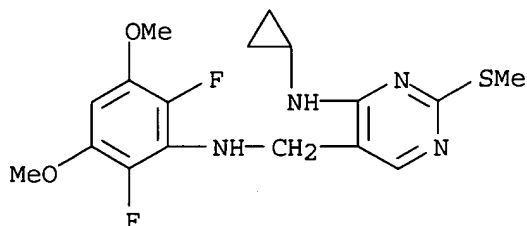
RN 651734-71-3 HCAPLUS

CN 5-Pyrimidinemethanamine, N-(2,6-difluoro-3,5-dimethoxyphenyl)-4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



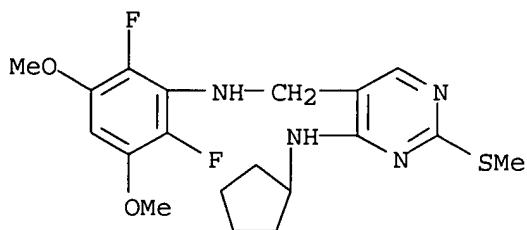
RN 651734-72-4 HCAPLUS

CN 5-Pyrimidinemethanamine, 4-(cyclopropylamino)-N-(2,6-difluoro-3,5-dimethoxyphenyl)-2-(methylthio)- (9CI) (CA INDEX NAME)



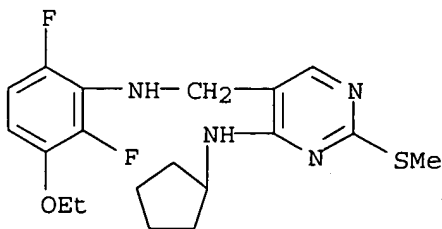
RN 651734-73-5 HCAPLUS

CN 5-Pyrimidinemethanamine, 4-(cyclopentylamino)-N-(2,6-difluoro-3,5-dimethoxyphenyl)-2-(methylthio)- (9CI) (CA INDEX NAME)



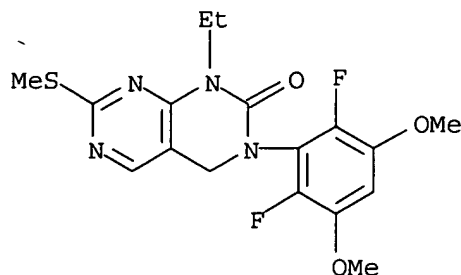
RN 651734-74-6 HCAPLUS

CN 5-Pyrimidinemethanamine, 4-(cyclopentylamino)-N-(3-ethoxy-2,6-difluorophenyl)-2-(methylthio)- (9CI) (CA INDEX NAME)



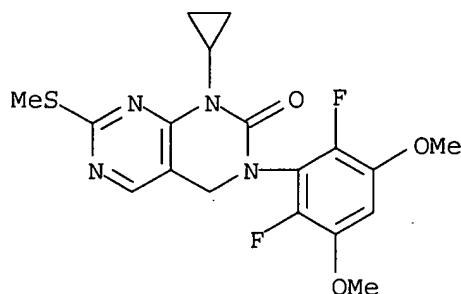
RN 651734-75-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-difluoro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro-7-(methylthio)- (9CI) (CA INDEX NAME)



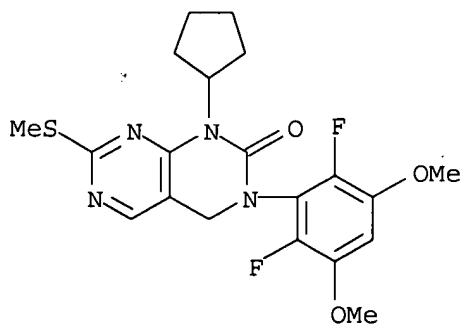
RN 651734-76-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopropyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylthio)- (9CI) (CA INDEX NAME)



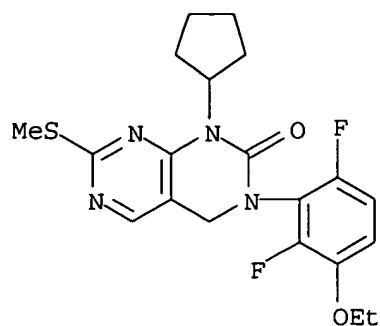
RN 651734-77-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylthio)- (9CI) (CA INDEX NAME)



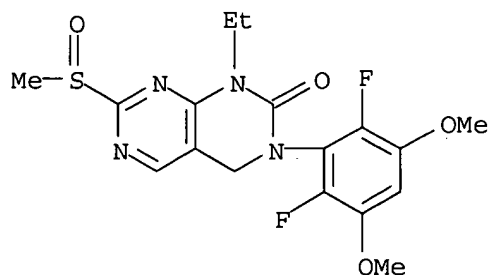
RN 651734-79-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(3-ethoxy-2,6-difluorophenyl)-3,4-dihydro-7-(methylthio)- (9CI) (CA INDEX NAME)



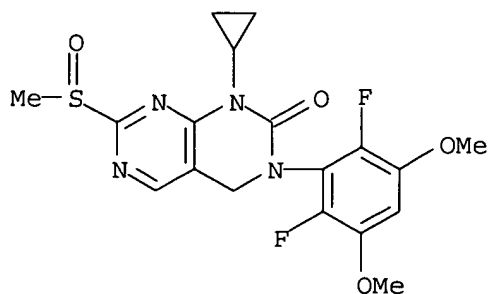
RN 651734-81-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-difluoro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro-7-(methylsulfinyl)- (9CI) (CA INDEX NAME)



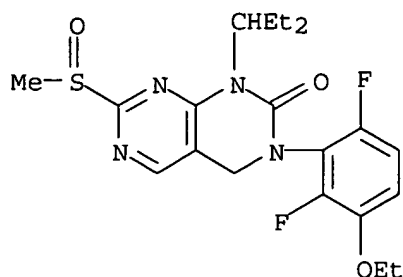
RN 651734-83-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopropyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylsulfinyl)- (9CI) (CA INDEX NAME)



RN 651734-86-0 HCAPLUS

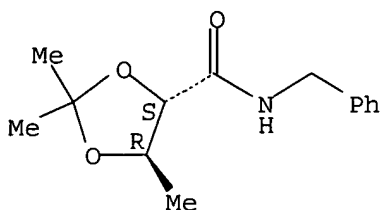
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(3-ethoxy-2,6-difluorophenyl)-1-(1-ethylpropyl)-3,4-dihydro-7-(methylsulfinyl)- (9CI) (CA INDEX NAME)



RN 651734-88-2 HCAPLUS

CN 1,3-Dioxolane-4-carboxamide, 2,2,5-trimethyl-N-(phenylmethyl)-, (4S,5R)-
(9CI) (CA INDEX NAME)

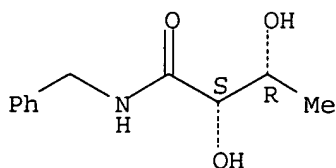
Absolute stereochemistry.



RN 651734-90-6 HCAPLUS

CN Butanamide, 2,3-dihydroxy-N-(phenylmethyl)-, (2S,3R)- (9CI) (CA INDEX
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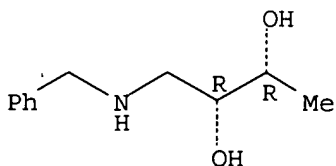
Absolute stereochemistry.



RN 651734-92-8 HCAPLUS

CN 2,3-Butanediol, 1-[(phenylmethyl)amino]-, (2R,3R)- (9CI) (CA INDEX NAME)

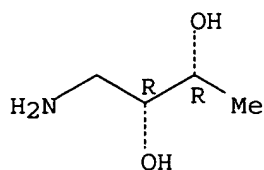
Absolute stereochemistry.



RN 651734-94-0 HCAPLUS

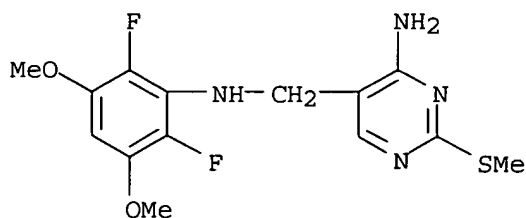
CN 2,3-Butanediol, 1-amino-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



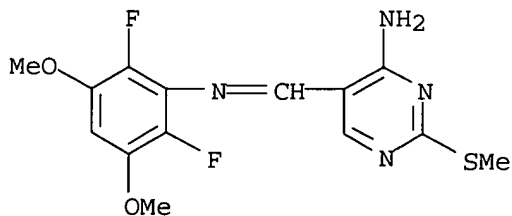
RN 651735-06-7 HCAPLUS

CN 5-Pyrimidinemethanamine, 4-amino-N-(2,6-difluoro-3,5-dimethoxyphenyl)-2-(methylthio)- (9CI) (CA INDEX NAME)



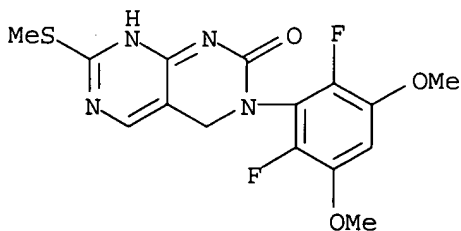
RN 651735-08-9 HCAPLUS

CN 4-Pyrimidinamine, 5-[[[(2,6-difluoro-3,5-dimethoxyphenyl)imino]methyl]-2-(methylthio)- (9CI) (CA INDEX NAME)



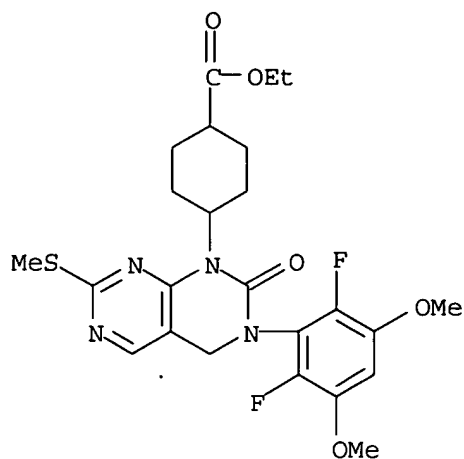
RN 651735-10-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylthio)- (9CI) (CA INDEX NAME)



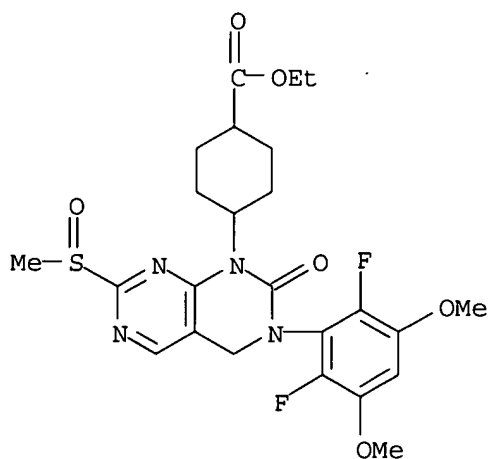
RN 651735-13-6 HCAPLUS

CN Cyclohexanecarboxylic acid, 4-[3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylthio)-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]-, ethyl ester (9CI) (CA INDEX NAME)



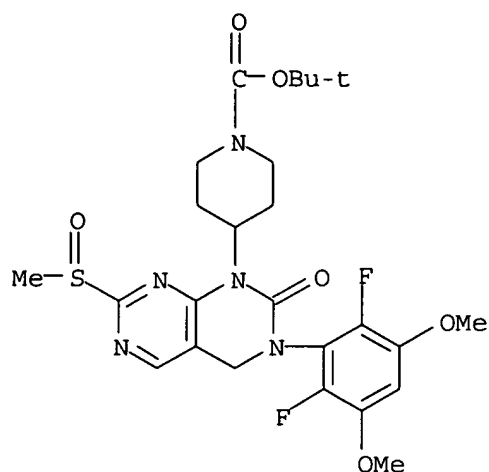
RN 651735-14-7 HCAPLUS

CN Cyclohexanecarboxylic acid, 4-[3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylsulfinyl)-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]-, ethyl ester (9CI) (CA INDEX NAME)



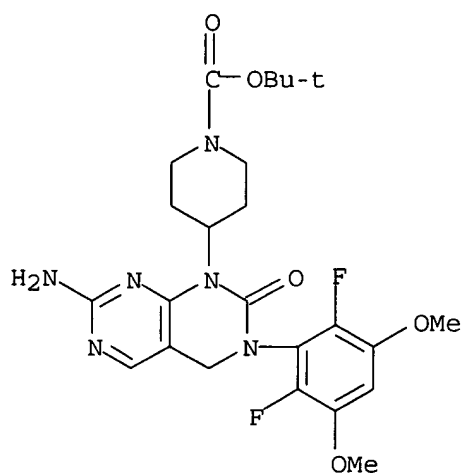
RN 651735-15-8 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylsulfinyl)-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



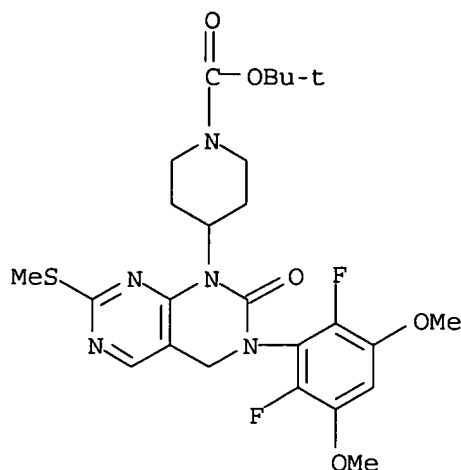
RN 651735-18-1 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[7-amino-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 651735-20-5 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylthio)-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



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ACCESSION NUMBER: 2002:123003 HCAPLUS

DOCUMENT NUMBER: 136:183833

TITLE: Preparation of 2-(4-pyridyl)amino-6-dialkoxyphenyl-pyrido[2,3-d]pyrimidin-7-ones as novel antiangiogenic agents useful for the treatment of diseases associated with aberrant blood vessel proliferation.

INVENTOR(S): Hamby, James Marino; Klutchko, Sylvester; Kramer, James Bernard

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 51 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2002012238 | A2 | 20020214 | WO 2001-US22881 | 20010720 |
| WO 2002012238 | A3 | 20020510 | | |
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| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2417942 | AA | 20020214 | CA 2001-2417942 | 20010720 |
| AU 2001077032 | A5 | 20020218 | AU 2001-77032 | 20010720 |
| EP 1307450 | A2 | 20030507 | EP 2001-954811 | 20010720 |
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| JP 2004519422 | T2 | 20040702 | JP 2002-518213 | 20010720 |
| BR 2001012857 | A | 20050209 | BR 2001-12857 | 20010720 |
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WO 2001-US22881

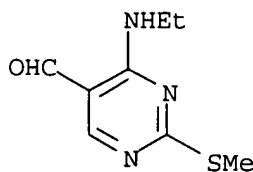
W 20010720

OTHER SOURCE(S):
GI

MARPAT 136:183833

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

- AB The invention discloses the preparation and the use of title compds. I, wherein: R1, R2, R5, R6 = H, halogen, alkyl, alkoxy, thio, thioalkyl, hydroxy, alkanoyl, nitrile, nitro, alkanoyloxy, CF3, alkyl ester, NH2 or derivs., aminoalkoxy, etc.; R3, R4 = alkyl, or haloalkyl; R7 = H, alkyl, alkenyl, alkynyl, or cycloalkyl; including their pharmaceutically acceptable salts and compns. as antiangiogenic agents. Compds. I, are useful for treating diseases, resulting from uncontrolled cellular proliferation such as cancer, atherosclerosis, rheumatoid arthritis, and psoriasis. The invention compds. exhibited greater selectivity for **inhibiting** VEGF and FGF, without **inhibiting** the Src family c-Src and Lck **kinases**. Claims include 12 specific compds. and the syntheses of 5 especially preferred compds. are described. For example, condensation of 3,5-dimethoxyphenylacetonitrile with aldehyde II, followed by acylation of the resultant imine, hydrolysis, oxidation, and sulfoxide displacement with the lithium salt of 4-amino-2,6-dimethoxypyridine, provided the most preferred compound III in 5 steps. Tyrosine **kinase inhibition** data (IC50 = μ M) was disclosed for compound I (R1, R5, R6 = H; R2 = 3-Cl; R3, R4 = Me; and R7 = Et) against: FGFR = 0.0002, VEGF-2 = 0.003, PDGF = 5, Lck = 2.77, and c-Src = >4. **Inhibition** of serum-stimulated HUVEC cell proliferation data (IC50 = μ M) of compound I (R1, R2, R5, R6 = H; R3, R4 = Me; and R7 = Et) against HUVEC = 0.009, A90 = 2.92, and C6 = >25 μ M was also provided. Metabolic stability and transport studies of compound I (R1, R2, R5, R6 = H; R3, R4 = Me; and R7 = Et) with human and mice liver S9 preps. indicated half-lives > 200 min. Also investigated, the in vivo anticancer efficacy of compound I (R1, R2, R5, R6 = H; R3, R4 = Me; and R7 = Et) against mammary adenocarcinoma M16/C: at 5 mg/kg dosage yielded a median mass of treated tumors/median mass of control tumor ratio of 39% with a net gain in subject body weight
- IT **185040-35-1P**, 4-Ethylamino-2-methylsulfanylpuridine-5-carboxaldehyde
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of pyrido[2,3-d]pyrimidine-7-ones as antiangiogenic agents)
- RN 185040-35-1 HCAPLUS
- CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)

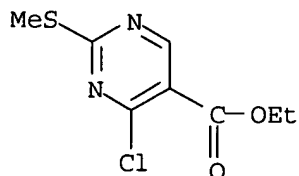


- IT **5909-24-0**, Ethyl 4-chloro-2-(methylthio)-5-pyrimidinecarboxylate
RL: RCT (Reactant); RACT (Reactant or reagent)

(precursor; preparation of pyrido[2,3-d]pyrimidine-7-ones as antiangiogenic agents)

RN 5909-24-0 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-chloro-2-(methylthio)-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



IT 144697-17-6, c-Src **kinase**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of pyrido[2,3-d]pyrimidine-7-ones as antiangiogenic agents)

RN 144697-17-6 HCAPLUS

CN Kinase (phosphorylating), gene c-src protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L23 ANSWER 4 OF 17 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:47493 HCAPLUS

DOCUMENT NUMBER: 132:175450

TITLE: Anti-angiogenic activity of selected receptor tyrosine **kinase inhibitors**, PD166285 and PD173074: Implications for combination treatment with photodynamic therapy

AUTHOR(S): Dimitroff, Charles J.; Klohs, Wayne; Sharma, Amarnath; Pera, Paula; Driscoll, Denise; Veith, Jean; Steinkampf, Randall; **Schroeder, Mel**; Klutchnko, Sylvester; Sumlin, Adam; Henderson, Barbara; Dougherty, Thomas J.; Bernacki, Ralph J.

CORPORATE SOURCE: Harvard Skin Disease Research Center, Harvard Medical School, Boston, MA, USA

SOURCE: Investigational New Drugs (1999), 17(2), 121-135

CODEN: INNDDK; ISSN: 0167-6997

PUBLISHER: Kluwer Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Angiogenesis, the formation of new blood vessels from an existing vasculature, is requisite for tumor growth. It entails intercellular coordination of endothelial and tumor cells through angiogenic growth factor signaling. Interruption of these events has implications in the suppression of tumor growth. PD166285, a broad-spectrum receptor tyrosine **kinase** (RTK) **inhibitor**, and PD173074, a selective FGFR1TK **inhibitor**, were evaluated for their anti-angiogenic activity and anti-tumor efficacy in combination with photodynamic therapy (PDT). To evaluate the anti-angiogenic and anti-tumor activities of these compds., RTK assays, in vitro tumor cell growth and microcapillary formation assays, in vivo murine angiogenesis and anti-tumor efficacy studies utilizing RTK **inhibitors** in combination with photodynamic therapy were performed. PD166285 **inhibited** PDGFR- β -, EGFR- and FGFR1TKs, and c-src TK by 50% (IC50) at concns. between 7-85 nM. PD173074 displayed selective **inhibitory** activity towards FGFR1TK at 26 nM. PD173074 demonstrated (> 100 fold) selective growth **inhibitory** action towards human umbilical vein

endothelial cells compared with a panel of tumor cell lines. Both PD166285 and PD173074 (at 10 nM) **inhibited** the formation of microcapillaries on Matrigel-coated plastic. In vivo anti-angiogenesis studies in mice revealed that oral administration (p.o.) of either PD166285 (1-25 mg/kg) or PD173074 (25-100 mg/kg) generated dose dependent **inhibition** of angiogenesis. Against a murine mammary 16c tumor, prolonged tumor regressions were achieved with daily p.o. doses of PD166285 (5-10 mg/kg) or PD173074 (30-60 mg/kg) following PDT compared with PDT alone. Many long-term survivors were also noted in combination treatment groups. PD166285 and PD173074 displayed potent anti-angiogenic and anti-tumor activity and prolonged the duration of anti-tumor response to PDT. Interference in membrane signal transduction by **inhibitors** of specific RTKs (e.g. FGFR1TK) should result in new chemotherapeutic agents having the ability to limit tumor angiogenesis and regrowth following cytoreductive treatments such as PDT.

IT **144697-17-6, c-Src tyrosine kinase**

RL: BOC (Biological occurrence); BSU (Biological study, unclassified);

BIOL (Biological study); OCCU (Occurrence)

(anti-angiogenic activity of selected receptor tyrosine **kinase**

inhibitors, in combination with photodynamic therapy)

RN 144697-17-6 HCAPLUS

CN Kinase (phosphorylating), gene c-src protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 5 OF 17 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:764041 HCAPLUS

DOCUMENT NUMBER: 132:22971

TITLE: Preparation of oxopyrido- and -pyrimidopyrimidines as cellular proliferation **inhibitors**

INVENTOR(S): Dobrusin, Ellen Myra; **Hamby, James Marino**; Kramer, James Bernard; **Schroeder, Mel Conrad**; Showalter, Howard Daniel Hollis; Toogood, Peter; Trumpf-Kallmeyer, Susanne A.

PATENT ASSIGNEE(S): Warner-Lambert Co.; USA

SOURCE: PCT Int. Appl., 133 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

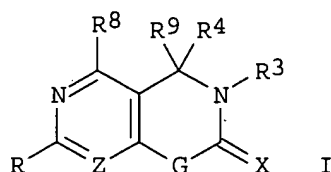
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|--|----------|-----------------|----------|
| WO 9961444 | A2 | 19991202 | WO 1999-US10187 | 19990510 |
| WO 9961444 | A3 | 20000203 | | |
| W: | AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2329703 | AA | 19991202 | CA 1999-2329703 | 19990510 |
| AU 9940734 | A1 | 19991213 | AU 1999-40734 | 19990510 |
| AU 763839 | B2 | 20030731 | | |
| BR 9911590 | A | 20010213 | BR 1999-11590 | 19990510 |

| | | | | |
|---|----|----------|-------------------|-------------|
| EP 1080092 | A2 | 20010307 | EP 1999-924165 | 19990510 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| TR 200003429 | T2 | 20010723 | TR 2000-200003429 | 19990510 |
| JP 2002516327 | T2 | 20020604 | JP 2000-550849 | 19990510 |
| EE 200000706 | A | 20020617 | EE 2000-706 | 19990510 |
| NZ 508268 | A | 20040227 | NZ 1999-508268 | 19990510 |
| ZA 2000006536 | A | 20020211 | ZA 2000-6536 | 20001110 |
| BG 104960 | A | 20011031 | BG 2000-104960 | 20001117 |
| HR 2000000799 | A1 | 20010630 | HR 2000-799 | 20001120 |
| NO 2000005928 | A | 20001123 | NO 2000-5928 | 20001123 |
| HK 1039483 | A1 | 20040618 | HK 2001-107828 | 20011108 |
| US 2004044012 | A1 | 20040304 | US 2003-638848 | 20030811 |
| PRIORITY APPLN. INFO.: | | | US 1998-86708P | P 19980526 |
| | | | US 1999-126158P | P 19990325 |
| | | | WO 1999-US10187 | W 19990510 |
| | | | US 2000-623737 | A3 20000907 |

OTHER SOURCE(S): MARPAT 132:22971
GI

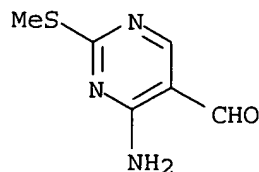


AB Title compds. [I; G = NR₂ or CHR₂; R = NHR₁ or SOO-2R₁; R₁,R₂ = H, (cyclo)alkyl, (un)substituted PH, -pyridyl, etc.; R₃ = groups cited for R₁, OH, alkoxy(carbonyl), etc.; R₄ = H; R₃R₄ = bond; R₈,R₉ = H, halo, NH₂, alkoxy carbonyl, etc.; X = O, S, (alkyl)imino, etc.; Z =N or CH] were prepared as cyclin-dependant and tyrosine **kinase inhibitors**. Thus, 5-aminomethyl-4-cyclopentylamino-2-methylthiopyrimidine (preparation given) was cyclocondensed with 1,1'-carbonyldiimidazole and the oxidized product aminated by 4-(MeO)C₆H₄NH₂ to give I [G = cyclopentylimino, R = 4-(MeO)C₆H₄NH, R₃ = R₄ = R₈ = R₉ = H, X = O]. Data for biol. activity of I were given.

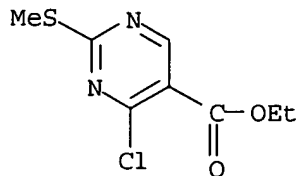
IT 770-31-0 5909-24-0 27431-62-5,
4-Diethylaminobutylamine 185040-35-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of bicyclic pyrimidines and bicyclic 3,4-dihydropyrimidines as **inhibitors** of cellular proliferation)

RN 770-31-0 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI)
(CA INDEX NAME)



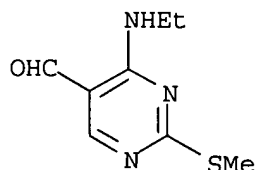
RN 5909-24-0 HCAPLUS
CN 5-Pyrimidinecarboxylic acid, 4-chloro-2-(methylthio)-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 27431-62-5 HCAPLUS
CN 1,4-Butanediamine, N,N-diethyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$\text{H}_2\text{N}-(\text{CH}_2)_4-\text{NEt}_2$

RN 185040-35-1 HCAPLUS
CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



L23 ANSWER 6 OF 17 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:561587 HCAPLUS

DOCUMENT NUMBER: 131:184962

TITLE: Preparation of oxidoamino-substituted
pyrido[2,3-d]pyrimidines as protein tyrosine
kinase inhibitors

INVENTOR(S): Doherty, Annette Marian; Hallak, Hussein Osman;
Hamby, James Marino

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: U.S., 25 pp.
CODEN: USXXAM

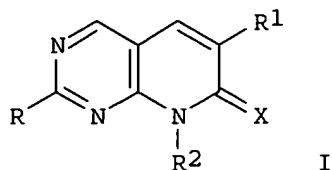
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--------|------------|-----------------|------------|
| US 5945422 | A | 19990831 | US 1998-15739 | 19980129 |
| PRIORITY APPLN. INFO.: | | | US 1997-38822P | P 19970205 |
| OTHER SOURCE(S): | MARPAT | 131:184962 | | |
| GI | | | | |



AB Title compds. [I; R = ONR5R6Z1Z2NH; R1 = (un)substituted Ph or heteroaryl; R2 = H, (cyclo)alkyl, phenyl(alkyl), heteroaryl, etc.; R5,R6 = H, alkyl, phenyl(alkyl), etc.; R5R6 = atoms to complete a ring; X = O, S, (acyl)imino; Z1,Z2 = bond, alkylene(oxy), -(thio), arylene] were prepared. Thus, I (R1 = C6H3Cl2-2,6, R2 = Me, X = O) (II; R = SMe) was aminated by Et2NCH2CH2OC6H4(NH2)-4 and the product oxidized to give II [R = 4-(ONEt2CH2CH2O)C6H4NH]. Data for biol. activity of I were given.

IT 100-46-9, Benzylamine, reactions 5909-24-0, Ethyl 4-chloro-2-methylthiopyrimidine-5-carboxylate 27431-62-5, 4-Diethylaminobutylamine

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of oxidoamino-substituted pyrido[2,3-d]pyrimidines as protein tyrosine **kinase inhibitors**)

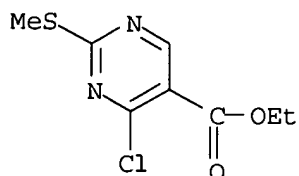
RN 100-46-9 HCAPLUS

CN Benzenemethanamine (9CI) (CA INDEX NAME)

H₂N-CH₂-Ph

RN 5909-24-0 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-chloro-2-(methylthio)-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 27431-62-5 HCAPLUS

CN 1,4-Butanediamine, N,N-diethyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

H₂N-(CH₂)₄-NEt₂

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 7 OF 17 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:139846 HCAPLUS

DOCUMENT NUMBER: 130:196643

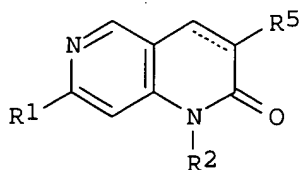
TITLE: Preparation of naphthyridinones as protein tyrosine **kinase** and cyclin dependant **kinase inhibitors**

INVENTOR(S): Barvian, Mark Robert; Denny, William Alexander;

Dobrusin, Ellen Myra; **Hamby, James Marino**;
 Showalter, Howard Daniel Hollis; Thompson, Andrew
 Mark; Winters, Roy Thomas; Wu, Zhipei
 PATENT ASSIGNEE(S): Warner-Lambert Company, USA
 SOURCE: PCT Int. Appl., 133 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 9909030 | A1 | 19990225 | WO 1998-US16848 | 19980813 |
| W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2291222 | AA | 19990225 | CA 1998-2291222 | 19980813 |
| CA 2291222 | C | 20040330 | | |
| AU 9888289 | A1 | 19990308 | AU 1998-88289 | 19980813 |
| AU 742999 | B2 | 20020117 | | |
| EP 1003745 | A1 | 20000531 | EP 1998-939941 | 19980813 |
| EP 1003745 | B1 | 20041229 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| BR 9811956 | A | 20000815 | BR 1998-11956 | 19980813 |
| JP 2001515078 | T2 | 20010918 | JP 2000-509710 | 19980813 |
| NZ 502704 | A | 20020628 | NZ 1998-502704 | 19980813 |
| AT 286053 | E | 20050115 | AT 1998-939941 | 19980813 |
| ZA 9807491 | A | 19990421 | ZA 1998-7491 | 19980819 |
| MX 9911792 | A | 20000630 | MX 1999-11792 | 19991215 |
| US 6150359 | A | 20001121 | US 2000-463553 | 20000126 |
| PRIORITY APPLN. INFO.: | | | US 1997-56746P | P 19970820 |
| | | | WO 1998-US16848 | W 19980813 |

OTHER SOURCE(S): MARPAT 130:196643
 GI



AB Title compds. [I; R1 = halo or (un)substituted amino; R2 = (bi)(cyclo)alkyl; R5 = H, halo, (hetero)aryl, etc.; dashed line = optional bond] were prepared. Thus, 4,6-diamino-3-pyridinecarboxaldehyde (preparation given) was cyclocondensed with 2,6-Cl₂C₆H₃CH₂CN and the major product treated with NaNO₂/HBF₄ to give, after N-methylation, major product I (R2 = Me, R5 = C₆H₃Cl₂-2,6) (II; R1 = F) which was aminated to give II (R1 =

e.g., NHMe). Data for biol. activity of I were given.
IT 27431-62-5, 4-Diethylaminobutylamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of naphthyridinones as protein tyrosine **kinase** and
cyclin dependant **kinase inhibitors**)
RN 27431-62-5 HCAPLUS
CN 1,4-Butanediamine, N,N-diethyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

H₂N-(CH₂)₄-NEt₂

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 8 OF 17 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:724585 HCAPLUS

DOCUMENT NUMBER: 130:90084

TITLE: Crystal structure of an angiogenesis **inhibitor**
bound to the FGF receptor tyrosine **kinase**
domain

AUTHOR(S): Mohammadi, Moosa; Froum, Scott; **Hamby, James**
M.; Schroeder, Mel C.; Panek, Robert
L.; Lu, Gina H.; Eliseenkova, Anna V.; Green, David;
Schlessinger, Joseph; Hubbard, Stevan R.

CORPORATE SOURCE: Departments of Pharmacology and Medicine, Kaplan
Comprehensive Cancer Center, and Skirball Institute of
Biomolecular Medicine, New York University Medical
Center, New York, NY, 10016, USA

SOURCE: EMBO Journal (1998), 17(20), 5896-5904

CODEN: EMJODG; ISSN: 0261-4189

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Angiogenesis, the sprouting of new blood vessels from pre-existing ones,
is an essential physiol. process in development, yet also plays a major
role in the progression of human diseases such as diabetic retinopathy,
atherosclerosis and cancer. The effects of the most potent angiogenic
factors, vascular endothelial growth factor (VEGF), angiopoietin and
fibroblast growth factor (FGF) are mediated through cell surface receptors
that possess intrinsic protein tyrosine **kinase** activity. In
this report, the authors describe a synthetic compound of the
pyrido[2,3-d]pyrimidine class, designated PD 173074, that selectively
inhibits the tyrosine **kinase** activities of the FGF and
VEGF receptors. The authors show that systemic administration of PD
173074 in mice can effectively block angiogenesis induced by either FGF or
VEGF with no apparent toxicity. To elucidate the determinants of
selectivity, the authors have determined the crystal structure of PD 173074 in
complex with the tyrosine **kinase** domain of FGF receptor 1 at 2.5
Å resolution. A high degree of surface complementarity between PD 173074
and the hydrophobic, ATP-binding pocket of FGF receptor 1 underlies the
potency and selectivity of this **inhibitor**. PD 173074 is thus a
promising candidate for a therapeutic angiogenesis **inhibitor** to
be used in the treatment of cancer and other diseases whose progression is
dependent upon new blood vessel formation.

IT 62031-54-3, Fibroblast growth factor
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(crystal structure of an angiogenesis **inhibitor** bound to the

FGF receptor tyrosine **kinase** domain)
RN 62031-54-3 HCAPLUS
CN Fibroblast growth factor (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 9 OF 17 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:600713 HCAPLUS

DOCUMENT NUMBER: 129:316187

TITLE: Synthesis and Tyrosine **Kinase**
Inhibitory Activity of a Series of
2-Amino-8H-pyrido[2,3-d]pyrimidines: Identification of
Potent, Selective Platelet-Derived Growth Factor
Receptor Tyrosine **Kinase Inhibitors**

AUTHOR(S): Boschelli, Diane H.; Wu, Zhipei; Klutchko, Sylvester
R.; Showalter, H. D. Hollis; **Hamby, James M.**
; Lu, Gina H.; Major, Terry C.; Dahring, Tawny K.;
Batley, Brian; Panek, Robert L.; Keiser, Joan; Hartl,
Brian G.; Kraker, Alan J.; Klohs, Wayne D.; Roberts,
Bill J.; Patmore, Sandra; Elliott, William L.;
Steinkampf, Randy; Bradford, Laura A.; Hallak,
Hussein; Doherty, Annette M.

CORPORATE SOURCE: Department of Medicinal Chemistry, Parke-Davis
Pharmaceutical Research Division of Warner-Lambert
Company, Ann Arbor, MI, 48105, USA

SOURCE: Journal of Medicinal Chemistry (1998), 41(22),
4365-4377

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

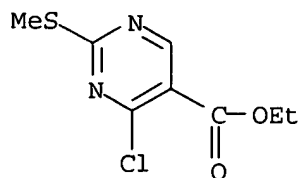
AB Screening of a compound library led to the identification of
2-amino-6-(2,6-dichlorophenyl)-8-methylpyrido[2,3-d]pyrimidine (I) as a
inhibitor of the platelet-derived growth factor receptor (PDGFr),
fibroblast growth factor receptor (FGFr), and c-src tyrosine
kinases (TKs). Replacement of the primary amino group at C-2 of I
with a 4-(N,N-diethylaminoethoxy)phenylamino group gave a compound, which
had greatly increased activity against all three TKs. In the present
work, variation of the aromatic group at C-6 and of the alkyl group at N-8 of
the pyrido[2,3-d]pyrimidine core provided several analogs that retained
potency, including derivs. that were biased toward **inhibition** of
the TK activity of PDGFr. Analogs of the 4-[(N,N-
diethylaminoethoxy)phenylamino]-substituted derivative with a 3-thiophene or
an unsubstituted Ph group at C-6 were the most potent **inhibitors**
. One compound, 2-[4-[2-(diethylamino)ethoxy]phenylamino]-8-ethyl-6-phenyl-
8H-pyrido[2,3-d]pyrimidin-7-one had IC50 values of 31, 88, and 31 nM
against PDGFr, FGFr, and c-src TK activity, resp.,. It was active in a
variety of PDGF-dependent cellular assay and blocked the in vivo growth of
three PDGF-dependent tumor lines.

IT 5909-24-0 185040-35-1

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and tyrosine **kinase inhibitory** activity of
aminopyrido[2,3-d]pyrimidines)

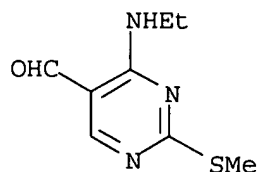
RN 5909-24-0 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-chloro-2-(methylthio)-, ethyl ester (6CI,
7CI, 8CI, 9CI) (CA INDEX NAME)



RN 185040-35-1 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 10 OF 17 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:496546 HCAPLUS

DOCUMENT NUMBER: 129:211390

TITLE: 2-Substituted Aminopyrido[2,3-d]pyrimidin-7(8H)-ones.
Structure-Activity Relationships Against Selected
Tyrosine **Kinases** and in Vitro and in Vivo
Anticancer Activity

AUTHOR(S): Klutchko, Sylvester R.; Hamby, James M.;
Boschelli, Diane H.; Wu, Zhipei; Kraker, Alan J.;
Amar, Aneesa M.; Hartl, Brian G.; Shen, Cynthia;
Klohs, Wayne D.; Steinkampf, Randall W.; Driscoll,
Denise L.; Nelson, James M.; Elliott, William L.;
Roberts, Billy J.; Stoner, Chad L.; Vincent, Patrick
W.; Dykes, Donald J.; Panek, Robert L.; Lu, Gina H.;
Major, Terry C.; Dahring, Tawny K.; Hallak, Hussein;
Bradford, Laura A.; Showalter, H. D. Hollis; Doherty,
Annette M.

CORPORATE SOURCE: Departments of Chemistry Cancer Research Vascular and
Cardiac Diseases and Pharmacokinetics and Drug
Metabolism Parke-Davis Pharmaceutical Research
Division, Warner-Lambert Company, Ann Arbor, MI,
48105, USA

SOURCE: Journal of Medicinal Chemistry (1998), 41(17),
3276-3292

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB While engaged in therapeutic intervention against a number of proliferative diseases, we have discovered the 2-aminopyrido[2,3-d]pyrimidin-7(8H)-ones as a novel class of potent, broadly active tyrosine **kinase** (TK) **inhibitors**. An efficient route was developed that enabled the synthesis of a wide variety of analogs with substitution on several positions of the template. Compds. of this series were competitive with

ATP and displayed submicromolar to low nanomolar potency against a panel of TKs, including receptor (platelet-derived growth factor, PDGFr; fibroblast growth factor, FGFr; epidermal growth factor, EGFr) and nonreceptor (c-Src) classes. One of the more thoroughly evaluated members was 63 with IC50 values of 0.079 μ M (PDGFr), 0.043 μ M (bFGFr), 0.044 μ M (EGFr), and 0.009 μ M (c-Src). In cellular studies, 63 **inhibited** PDGF-mediated receptor autophosphorylation in a number of cell lines at IC50 values of 0.026-0.002 μ M and proliferation of two PDGF-dependent lines at 0.3 μ M. It also caused **inhibition** of soft agar colony formation in three cell lines that overexpress the c-Src TK, with IC50 values of 0.33-1.8 μ M. In in vivo studies against a panel of seven xenograft tumor models with known and/or inferred dependence on the EGFr, PDGFr, and c-Src TKs, compound 63 produced a tumor growth delay of 10.6 days against the relatively refractory SK-OV-3 ovarian xenograft and also displayed activity against the HT-29 tumor. In rat oral bioavailability studies, compound 63 plasma concns. declined in a biexponential manner, and systemic plasma clearance was high relative to liver blood flow. Finally, in rat metabolism studies, HPLC chromatog. identified two metabolites of 63. Because of the excellent potency of 63 against selected TKs, in vitro and in vivo studies are underway for this compound in addnl. tumor models dependent upon PDGFr, FGFr, and c-Src to assess its potential for advancement to clin. trials.

IT **144697-17-6**, c-Src tyrosine **kinase**
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (preparation of aminopyridopyrimidinones as tyrosine **kinase inhibitors** and anticancer agents)

RN 144697-17-6 HCAPLUS

CN Kinase (phosphorylating), gene c-src protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **100-46-9**, Benzylamine, reactions **5909-24-0**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of aminopyridopyrimidinones as tyrosine **kinase inhibitors** and anticancer agents)

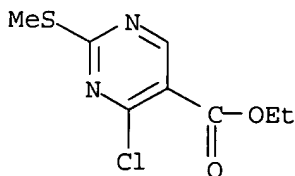
RN 100-46-9 HCAPLUS

CN Benzenemethanamine (9CI) (CA INDEX NAME)

H₂N-CH₂-Ph

RN 5909-24-0 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-chloro-2-(methylthio)-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

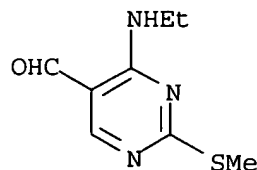


IT **185040-35-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of aminopyridopyrimidinones as tyrosine **kinase**

inhibitors and anticancer agents)

RN 185040-35-1 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA
INDEX NAME)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 11 OF 17 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:202673 HCAPLUS

DOCUMENT NUMBER: 128:257440

TITLE: Preparation of pyrido[2,3-d]pyrimidines for
inhibiting protein tyrosine **kinase**
mediated cellular proliferation

INVENTOR(S): Blankley, Clifton John; Boschelli, Diane Harris;
Doherty, Annette Marian; **Hamby, James Marino**
; Klutchko, Sylvester; Panek, Robert Lee

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: U.S., 39 pp., Cont.-in-part of U.S. 5,620,981.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| US 5733914 | A | 19980331 | US 1996-611279 | 19960403 |
| US 5620981 | A | 19970415 | US 1995-433294 | 19950503 |
| IL 117923 | A1 | 20000601 | IL 1996-117923 | 19960416 |
| CA 2214219 | AA | 19961107 | CA 1996-2214219 | 19960426 |
| WO 9634867 | A1 | 19961107 | WO 1996-US5819 | 19960426 |
| W: AU, BG, CA, CN, CZ, EE, GE, HU, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, UZ, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9655769 | A1 | 19961121 | AU 1996-55769 | 19960426 |
| AU 713727 | B2 | 19991209 | | |
| EP 823908 | A1 | 19980218 | EP 1996-913175 | 19960426 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI | | | | |
| CN 1183099 | A | 19980527 | CN 1996-193678 | 19960426 |
| CN 1083452 | B | 20020424 | | |
| JP 11504922 | T2 | 19990511 | JP 1996-533372 | 19960426 |
| NZ 307021 | A | 20010427 | NZ 1996-307021 | 19960426 |
| CZ 288160 | B6 | 20010516 | CZ 1997-3275 | 19960426 |
| EE 3770 | B1 | 20020617 | EE 1997-274 | 19960426 |
| PL 184093 | B1 | 20020830 | PL 1996-323089 | 19960426 |
| SK 283952 | B6 | 20040608 | SK 1997-1410 | 19960426 |
| ZA 9603486 | A | 19961113 | ZA 1996-3486 | 19960502 |
| NO 9705033 | A | 19971031 | NO 1997-5033 | 19971031 |

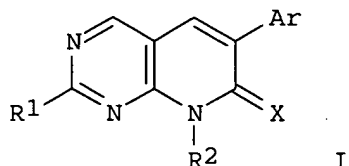
NO 310110
PRIORITY APPLN. INFO.:

B1 20010521

US 1995-433294
US 1996-611279
WO 1996-US5819

A2 19950503
A 19960403
W 19960426

OTHER SOURCE(S): MARPAT 128:257440
GI



AB The title compds. [I; X = NH, N-acyl, O, S; R1 = SOR3, SO2R3; R2, R3 = H, (CH2)nPh (where Ph = (un)substituted phenyl; n = 0-3), heteroarom., etc.; Ar = (un)substituted Ph, heteroaryl], **inhibitors** of protein tyrosine **kinases**, and thus useful in treating cellular proliferation, especially useful in treating cancer, atherosclerosis, restenosis, and psoriasis, were prepared and formulated. Thus, treatment of 2-ethoxyethanol with NaH followed by addition of 2,6-dimethylphenylacetonitrile, and 2-amino-4-methylamino-5-pyrimidinecarboxaldehyde (preparation described) afforded pyrido[2,3-d]pyrimidine I [R1 = NH2; R2 = Me; X = NH; Ar = 2,6-dimethylphenyl] which showed 42% **inhibition** of PDGFr-TK at 50 μ M.

IT 100-46-9, Benzylamine, reactions 5909-24-0

27431-62-5, 4-(Diethylamino)butylamine

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of pyrido[2,3-d]pyrimidines for **inhibiting** protein tyrosine **kinase** mediated cellular proliferation)

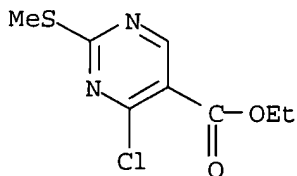
RN 100-46-9 HCAPLUS

CN Benzenemethanamine (9CI) (CA INDEX NAME)

H2N-CH2-Ph

RN 5909-24-0 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-chloro-2-(methylthio)-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 27431-62-5 HCAPLUS

CN 1,4-Butanediamine, N,N-diethyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

H2N-(CH2)4-NEt2

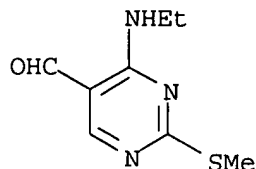
IT 185040-35-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyrido[2,3-d]pyrimidines for **inhibiting** protein tyrosine **kinase** mediated cellular proliferation)

RN 185040-35-1 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 12 OF 17 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:202672 HCAPLUS

DOCUMENT NUMBER: 128:257439

TITLE: Preparation of 6-arylpyrido[2,3-d]pyrimidines and naphthyridines for **inhibiting** protein tyrosine **kinase** mediated cellular proliferation

INVENTOR(S): Blankley, Clifton John; Doherty, Annette Marian; **Hamby, James Marino**; Panek, Robert Lee; **Schroeder, Mel Conrad**; Showalter, Howard Daniel Hollis; **Connolly, Cleo**

PATENT ASSIGNEE(S): USA

SOURCE: U.S., 36 pp., Cont.-in-part of U.S. Ser. No. 339,051, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

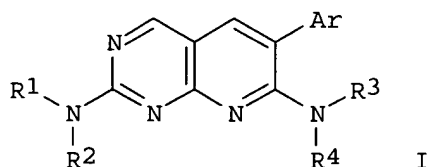
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

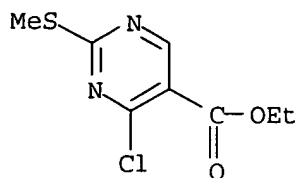
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 5733913 | A | 19980331 | US 1995-539410 | 19951106 |
| CA 2199964 | AA | 19960523 | CA 1995-2199964 | 19951113 |
| WO 9615128 | A2 | 19960523 | WO 1995-US14700 | 19951113 |
| W: AM, AU, BG, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LT, LV, MD, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, UA, UZ | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9641078 | A1 | 19960606 | AU 1996-41078 | 19951113 |
| AU 711426 | B2 | 19991014 | | |
| EP 790997 | A2 | 19970827 | EP 1995-939129 | 19951113 |
| EP 790997 | B1 | 20000322 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| HU 76853 | A2 | 19971229 | HU 1997-1511 | 19951113 |
| CN 1169726 | A | 19980107 | CN 1995-196230 | 19951113 |
| CN 1085666 | B | 20020529 | | |
| JP 10509452 | T2 | 19980914 | JP 1995-516240 | 19951113 |

| | | | | |
|------------------------|--------|------------|-----------------|-------------|
| CZ 286160 | B6 | 20000112 | CZ 1997-1390 | 19951113 |
| AT 190978 | E | 20000415 | AT 1995-939129 | 19951113 |
| PT 790997 | T | 20000630 | PT 1995-939129 | 19951113 |
| ES 2146782 | T3 | 20000816 | ES 1995-939129 | 19951113 |
| SK 281724 | B6 | 20010710 | SK 1997-609 | 19951113 |
| PL 181893 | B1 | 20011031 | PL 1995-320169 | 19951113 |
| MD 1861 | F2 | 20020228 | MD 1997-970187 | 19951113 |
| RU 2191188 | C2 | 20021020 | RU 1997-110269 | 19951113 |
| ZA 9509675 | A | 19960529 | ZA 1995-9675 | 19951114 |
| IL 115970 | A1 | 19990620 | IL 1995-115970 | 19951114 |
| BG 63162 | B1 | 20010531 | BG 1997-101326 | 19970313 |
| FI 9701953 | A | 19970512 | FI 1997-1953 | 19970507 |
| NO 9702198 | A | 19970513 | NO 1997-2198 | 19970513 |
| NO 308250 | B1 | 20000821 | | |
| US 5952342 | A | 19990914 | US 1998-40792 | 19980318 |
| GR 3033439 | T3 | 20000929 | GR 2000-401126 | 20000518 |
| PRIORITY APPLN. INFO.: | | | US 1994-339051 | B2 19941114 |
| | | | US 1995-539410 | A 19951106 |
| | | | WO 1995-US14700 | W 19951113 |
| OTHER SOURCE(S): | MARPAT | 128:257439 | | |
| GI | | | | |



- AB The title compds. [I; R1, R2, R4 = H, C1-8 alkyl, C2-8 alkenyl, etc.; R3 = C(O)R8, CO2R8, C(S)R8, etc.; R8 = H, C1-8 alkyl, C2-8 alkenyl, etc.; Ar = (un)substituted aromatic or heteroarom. selected from Ph, imidazolyl, pyrrolyl, etc.], **inhibitors of protein tyrosine kinase** which are especially useful in treating atherosclerosis, restenosis, psoriasis, as well as bacterial infections, were prepared and formulated. Thus, reaction of 2,7-diamino-6-(2,6-dichlorophenyl)pyrido[2,3-d]pyrimidine (preparation described) with tert-Bu isocyanate in the presence of NaH in DMF afforded the urea I [R1 = R4 = H; R2 = R3 = C(O)NHtBu; Ar = 2,6-Cl2C6H3] which showed IC50 of 10.2 μ M against PDGF receptor tyrosine **kinase**.
- IT **5909-24-0 27431-62-5**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of 6-arylpyrido[2,3-d]pyrimidines and naphthyridines for **inhibiting** protein tyrosine **kinase** mediated cellular proliferation)
- RN 5909-24-0 HCAPLUS
- CN 5-Pyrimidinecarboxylic acid, 4-chloro-2-(methylthio)-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 27431-62-5 HCAPLUS

CN 1,4-Butanediamine, N,N-diethyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

H₂N-(CH₂)₄-NEt₂

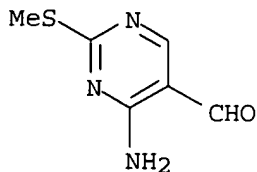
IT 770-31-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 6-arylpyrido[2,3-d]pyrimidines and naphthyridines for **inhibiting** protein tyrosine **kinase** mediated cellular proliferation)

RN 770-31-0 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 13 OF 17 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:686365 HCAPLUS

DOCUMENT NUMBER: 127:355051

TITLE: Discovery and structure-activity studies of a novel series of pyrido[2,3-d]pyrimidine tyrosine **kinase inhibitors**

AUTHOR(S): Connolly, Cleo J. C.; Hamby, James M.; Schroeder, Mel C.; Barvian, Mark; Lu, Gina H.; Panek, Robert L.; Amar, Aneesa; Shen, Cindy; Kraker, Alan J.; Fry, David W.; Klohs, Wayne D.; Doherty, Annette M.

CORPORATE SOURCE: Division of Warner-Lambert Company, Department of Chemistry, Parke-Davis Pharmaceutical Research, Ann Arbor, MI, 48105, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(18), 2415-2420

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 127:355051

AB The **inhibition** of tyrosine **kinase**-mediated signal transduction pathways represents a therapeutic approach to the intervention of proliferative diseases such as cancer, atherosclerosis, and restenosis. A novel series of pyrido[2,3-d]pyrimidine **inhibitors** of the PDGFr, bFGFr, and c-Src tyrosine **kinases** was developed from compound library screening and lead optimization. In addition, highly selective **inhibitors** of the FGFr tyrosine **kinase** were also discovered and developed from this novel series of pyrido[2,3-d]pyrimidines. The syntheses, biol. evaluation, and structure-activity relationships of this series are reported.

IT 144697-17-6, c-Src tyrosine **kinase**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(discovery and structure-activity studies of a novel series of pyrido[d]pyrimidine tyrosine **kinase inhibitors**)

RN 144697-17-6 HCAPLUS

CN Kinase (phosphorylating), gene c-src protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 14 OF 17 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:436125 HCAPLUS

DOCUMENT NUMBER: 127:117061

TITLE: Structure-Activity Relationships for a Novel Series of Pyrido[2,3-d]pyrimidine Tyrosine **Kinase Inhibitors**

AUTHOR(S): Hamby, James M.; Connolly, Cleo J.

C.; Schroeder, Mel C.; Winters, R.

Thomas; Showalter, H. D. Hollis; Panek, Robert L.; Major, Terry C.; Olsewski, Bronislawa; Ryan, Michael J.; Dahring, Tawny; Lu, Gina H.; Keiser, Joan; Amar, Aneesa; Shen, Cindy; Kraker, Alan J.; Slintak, Veronika; Nelson, James M.; Fry, David W.; Bradford, Laura; Hallak, Hussein; Doherty, Annette M.

CORPORATE SOURCE: Parke-Davis Pharmaceutical Research, Division of Warner Lambert Company, Ann Arbor, MI, 48105, USA

SOURCE: Journal of Medicinal Chemistry (1997), 40(15), 2296-2303

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Screening of a compound library for **inhibitors** of the fibroblast growth factor (FGFr) and platelet-derived growth factor (PDGFr) receptor tyrosine **kinases** led to the development of a novel series of ATP competitive pyrido[2,3-d]pyrimidine tyrosine **kinase inhibitors**. The initial lead, 1-[2-amino-6-(2,6-dichlorophenyl)pyrido[2,3-d]pyrimidin-7-yl]-3-tert-butylurea (I; PD-089828), was found to be a broadly active tyrosine **kinase inhibitor**. I **inhibited** the PDGFr, FGFr, EGFr, and c-src tyrosine **kinases** with IC50 values of 1.11, 0.13, 0.45, and 0.22 μ M, resp. Subsequent SAR studies led to the synthesis of new analogs with improved potency, solubility, and bioavailability relative to the initial lead. For example, the introduction of a [4-(diethylamino)butyl]amino side chain into the 2-position of I afforded a compound (II) with enhanced potency and bioavailability. II **inhibited** PDGF-stimulated vascular smooth muscle cell proliferation with an IC50 of 0.3 μ M.

Furthermore, replacement of the 6-(2,6-dichlorophenyl) moiety of I with a 6-(3',5'-dimethoxyphenyl) functionality produced a highly selective FGFR tyrosine **kinase inhibitor** (III). III **inhibited** the FGFR tyrosine **kinase** with an IC₅₀ of 0.060 μ M, whereas IC₅₀s for the **inhibition** of the PDGFR, FGFR, EGFR, c-src, and InsR tyrosine **kinases** for this compound were all greater than 50 μ M.

IT **144697-17-6**, c-Src tyrosine **kinase**
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (pyrido[2,3-d]pyrimidine tyrosine **kinase inhibitor** preparation and structure-activity relationship)

RN 144697-17-6 HCAPLUS

CN Kinase (phosphorylating), gene c-src protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **27431-62-5**, 4-(Diethylaminobutylamine)
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction; pyrido[2,3-d]pyrimidine tyrosine **kinase inhibitor** preparation and structure-activity relationship)

RN 27431-62-5 HCAPLUS

CN 1,4-Butanediamine, N,N-diethyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

H₂N-(CH₂)₄-NEt₂

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 15 OF 17 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:407661 HCAPLUS

DOCUMENT NUMBER: 127:130930

TITLE: **Inhibition** of growth factor-mediated tyrosine phosphorylation in vascular smooth muscle by PD 08928, a new synthetic protein tyrosine **kinase inhibitor**

AUTHOR(S): Dahring, Tawny K.; Lu, Gina H.; **Hamby, James M.**; Batley, Brain L.; Kraker, Alan J.; Panek, Robert L.

CORPORATE SOURCE: Departments of Vascular and Cardiac Diseases, Chemistry and Cancer Research, Division of Warner-Lambert Company, Parke-Davis Pharmaceutical Research, Ann Arbor, MI, 48105, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics (1997), 281(3), 1446-1456
 CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB PD 089828, a novel protein tyrosine **kinase inhibitory** of a new structural class, the 6-aryl-pyrido-[2,3-d]pyrimidines, was identified by screening a compound library with assays that measured protein tyrosine **kinase** activity. PD 089828 was found to **inhibit** human full-length fibroblast growth factor (FGF) receptor-1 (FGFR-1), platelet-derived growth factor (PDGF) receptor β subunit (PDGFR- β), Src nonreceptor tyrosine **kinase** (c-Src) and epidermal growth factor (EGF) receptor (EGFR) tyrosine **kinases** with half-maximal **inhibitory** potencies (IC₅₀ values) of 0.15,

0.18, 1.76 and 5.47 μ M, resp. PD 089828 was further characterized as an ATP competitive **inhibitor** of the growth factor receptor tyrosine **kinases** (FGFR-1, PDGFR- β and EGFR) but a noncompetitive **inhibitor** of c-Src tyrosine **kinase** with respect to ATP. In addition, PD 089828 **inhibited** PDGF- and EGF-stimulated receptor autophosphorylation in vascular smooth muscle cells (VSMC) and basic FGF-mediated tyrosine phosphorylation in A121 cells with IC₅₀ values similar to the potencies observed for **inhibitor** of receptor tyrosine **kinase** activity. The **inhibition** of PDGF receptor autophosphorylation in VSMC by PD 089828 occurred rapidly, with maximal effects reached within 5 min of drug exposure. **Inhibition** after single exposure was long lasting but also rapidly reversible, occurring within 5 min after drug removal. The PDGF-induced association of downstream signaling proteins, including phosphoinositide-3-**kinase** (PI-3K), growth factor receptor binding protein-2 (GRB2), SH-2 domain and collagen like (Shc) and phospholipase C γ (PLC γ), with VSMC PDGF receptors was also blocked as a result of the **inhibition** of PDGF-stimulated receptor autophosphorylation by PD 089828. PD 089828 also **inhibited** the PDGF-induced tyrosine phosphorylation of the 44- and 42-kDa mitogen-activated protein **kinase** isoforms. Moreover, the effects of PD 089828 were demonstrated in functional assays in which PDGF-stimulated DNA synthesis, PDGF-directed migration and serum-stimulated growth of VSMC were all **inhibited** to the same extent as PDGF receptor autophosphorylation (IC₅₀ = 0.8, 4.5 and 1.8 μ M, resp.). These results highlight the biol. characteristics of PD 089828 as a novel, broadly active protein tyrosine **kinase inhibitor** with long-lasting but reversible cellular effects. The potential therapeutic use of these broadly acting, nonselective **inhibitors** as antiproliferative and antimigratory agents could extend to such diseases as cancer, atherosclerosis and restenosis in which redundancies in growth-signaling pathways are known to exist.

IT 144697-17-6, c-Src tyrosine **kinase** 147014-97-9

, Cyclin-dependent **kinase**-4

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(**inhibition** of growth factor-mediated tyrosine phosphorylation in vascular smooth muscle by new synthetic protein tyrosine **kinase inhibitor** PD 08928 in relation to potential therapeutic use)

RN 144697-17-6 HCAPLUS

CN Kinase (phosphorylating), gene c-src protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 147014-97-9 HCAPLUS

CN Kinase (phosphorylating), protein p33CDK4 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L23 ANSWER 16 OF 17 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:26258 HCAPLUS

DOCUMENT NUMBER: 126:59965

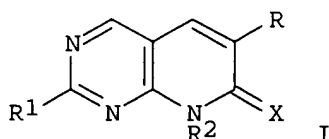
TITLE: Preparation of pyrido[2,3-d]pyrimidines as protein tyrosine **kinase** mediated cell proliferation **inhibitors**

INVENTOR(S): Blankley, Clifton John; Boschelli, Diane Harris; Doherty, Annette Marian; **Hamby, James Marino**; Klutchko, Sylvester; Panek, Robert Lee

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 147 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|------------|
| WO 9634867 | A1 | 19961107 | WO 1996-US5819 | 19960426 |
| W: AU, BG, CA, CN, CZ, EE, GE, HU, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, UZ, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5620981 | A | 19970415 | US 1995-433294 | 19950503 |
| US 5733914 | A | 19980331 | US 1996-611279 | 19960403 |
| AU 9655769 | A1 | 19961121 | AU 1996-55769 | 19960426 |
| AU 713727 | B2 | 19991209 | | |
| EP 823908 | A1 | 19980218 | EP 1996-913175 | 19960426 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI | | | | |
| JP 11504922 | T2 | 19990511 | JP 1996-533372 | 19960426 |
| NZ 307021 | A | 20010427 | NZ 1996-307021 | 19960426 |
| EE 3770 | B1 | 20020617 | EE 1997-274 | 19960426 |
| PL 184093 | B1 | 20020830 | PL 1996-323089 | 19960426 |
| SK 283952 | B6 | 20040608 | SK 1997-1410 | 19960426 |
| NO 9705033 | A | 19971031 | NO 1997-5033 | 19971031 |
| NO 310110 | B1 | 20010521 | | |
| PRIORITY APPLN. INFO.: | | | US 1995-433294 | A 19950503 |
| | | | US 1996-611279 | A 19960403 |
| | | | WO 1996-US5819 | W 19960426 |
| OTHER SOURCE(S): | | | MARPAT 126:59965 | |
| GI | | | | |



AB Title compds. [I; R = (un)substituted Ph or heteroaryl; R1 = NR3R4, SOO-2R3, OR3; R2-R4 = H, alkyl, (CH2)0-3Ph, heteroaryl, etc.; R4 may addnl. = COR3, CO2R3, SO2R3, etc.; NR3R4 = atoms to form a ring; X = O, S, (acyl)imino] were pred. Thus, EtOCH:C(CN)CO2Et was cyclocondensed with MeSC(:NH)NH2 and the product converted in 5 steps to 2-amino-4-methylamino-5-pyrimidinecarboxaldehyde which was cyclocondensed with 2,6-Me2C6H3CH2CN to give I (R = 2,6-Me2C6H3, R1 = NH2, R2 = Me, X = NH). Data for biol. activity of I were given.

IT 100-46-9, Benzylamine, reactions 5909-24-0
 27431-62-5, 4-Diethylaminobutylamine
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of pyrido[2,3-d]pyrimidines as protein tyrosine kinase mediated cell proliferation inhibitors)

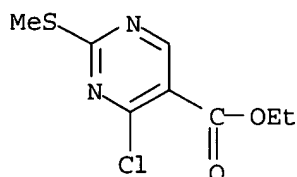
RN 100-46-9 HCAPLUS

CN Benzenemethanamine (9CI) (CA INDEX NAME)

H₂N-CH₂-Ph

RN 5909-24-0 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-chloro-2-(methylthio)-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 27431-62-5 HCAPLUS

CN 1,4-Butanediamine, N,N-diethyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

H₂N-(CH₂)₄-NEt₂

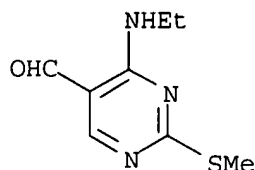
IT 185040-35-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyrido[2,3-d]pyrimidines as protein tyrosine **kinase** mediated cell proliferation **inhibitors**)

RN 185040-35-1 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-(ethylamino)-2-(methylthio)- (9CI) (CA INDEX NAME)



L23 ANSWER 17 OF 17 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:467130 HCAPLUS

DOCUMENT NUMBER: 125:114688

TITLE: Preparation of 6-aryl pyrido[2,3-d]pyrimidines and naphthyridines for **inhibiting** protein tyrosine **kinase**-mediated cellular proliferation

INVENTOR(S): Blankley, Clifton John; Doherty, Annette Marian; **Hamby, James Marino**; Panek, Robert Lee; **Schroeder, Mel Conrad**; Showalter, Howard Daniel Hollis; **Connolly, Cleo**

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 134 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

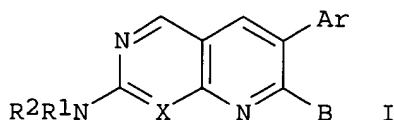
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 9615128 | A2 | 19960523 | WO 1995-US14700 | 19951113 |
| W: AM, AU, BG, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LT, LV, MD, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, UA, UZ | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5733913 | A | 19980331 | US 1995-539410 | 19951106 |
| AU 9641078 | A1 | 19960606 | AU 1996-41078 | 19951113 |
| AU 711426 | B2 | 19991014 | | |
| EP 790997 | A2 | 19970827 | EP 1995-939129 | 19951113 |
| EP 790997 | B1 | 20000322 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 10509452 | T2 | 19980914 | JP 1995-516240 | 19951113 |
| AT 190978 | E | 20000415 | AT 1995-939129 | 19951113 |
| SK 281724 | B6 | 20010710 | SK 1997-609 | 19951113 |
| PL 181893 | B1 | 20011031 | PL 1995-320169 | 19951113 |
| MD 1861 | F2 | 20020228 | MD 1997-970187 | 19951113 |
| RU 2191188 | C2 | 20021020 | RU 1997-110269 | 19951113 |
| BG 63162 | B1 | 20010531 | BG 1997-101326 | 19970313 |
| FI 9701953 | A | 19970512 | FI 1997-1953 | 19970507 |
| NO 9702198 | A | 19970513 | NO 1997-2198 | 19970513 |
| NO 308250 | B1 | 20000821 | | |
| GR 3033439 | T3 | 20000929 | GR 2000-401126 | 20000518 |
| PRIORITY APPLN. INFO.: | | | US 1994-339051 | A 19941114 |
| | | | US 1995-539410 | A 19951106 |
| | | | WO 1995-US14700 | W 19951113 |

OTHER SOURCE(S): MARPAT 125:114688
GI



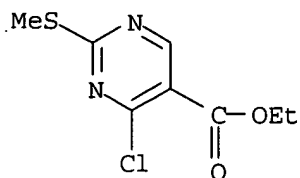
AB 6-Arylpyrido[2,3-d]pyrimidines and naphthyridines I [X = CH, N; B = halo, OH, NR3R4; R1, R2, R3, R4 = H, C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, Ar', amino, C1-8 alkylamino, di-C1-8 alkylamino, wherein the alkyl, alkenyl, and alkynyl groups may be substituted by amino, OH, or 5- or 6-membered carbocyclic or heterocyclic ring; Ar, Ar' = (un)substituted aromatic or heteroarom. groups; R1R2N or R3R4N can complete a ring having 3-6 C atoms and optionally containing 1 or 2 heteroatoms; when X = N and B = NR3R4, one of R3 and R4 ≠ H] or their pharmaceutically acceptable acid and base addition salts, useful as **inhibitors** of protein tyrosine **kinase** and thus useful in treating cellular proliferation mediated thereby, are claimed. The compds. are especially useful in treating atherosclerosis, restenosis, psoriasis, as well as bacterial infections. In an example, the IC50 of I [X = N, B = NHCONH2, R1 = H, R2 = Et2N(CH2)4 Ar = 2,6-Cl2C6H3; preparation given] for **inhibition** of protein tyrosine **kinases** was 0.231 μM for PDGF and 0.0954 for FGF.

IT 5909-24-0, Ethyl 4-chloro-2-methylthio-5-pyrimidinecarboxylate
27431-62-5, 4-(Diethylamino)butylamine

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aryl pyridopyrimidines and naphthyridines for
inhibiting protein tyrosine **kinase**-mediated cellular
proliferation)

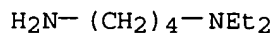
RN 5909-24-0 HCAPLUS

CN 5-Pyrimidinecarboxylic acid, 4-chloro-2-(methylthio)-, ethyl ester (6CI,
7CI, 8CI, 9CI) (CA INDEX NAME)



RN 27431-62-5 HCAPLUS

CN 1,4-Butanediamine, N,N-diethyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



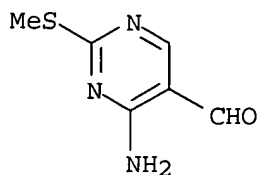
IT 770-31-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation of aryl pyridopyrimidines and naphthyridines for
inhibiting protein tyrosine **kinase**-mediated cellular
proliferation)

RN 770-31-0 HCAPLUS

CN 5-Pyrimidinecarboxaldehyde, 4-amino-2-(methylthio)- (6CI, 7CI, 8CI, 9CI)
(CA INDEX NAME)



=> d ibib abs hitstr 127 1-12

L27 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:120672 HCAPLUS

DOCUMENT NUMBER: 142:198094

TITLE: Preparation of pyrimidopyrimidines as protein kinase inhibitors

INVENTOR(S): Sim, Taebo; Lee, Hyun Soo; Ren, Pingda; Ding, Qiang; Wang, Xia; Uno, Tetsuo; Zhang, Guobao; Liu, Yi; Li, Bing; Li, Lintong; Gray, Nathaniel; You, Shuli

PATENT ASSIGNEE(S): IRM LLC, Bermuda

SOURCE: PCT Int. Appl., 148 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

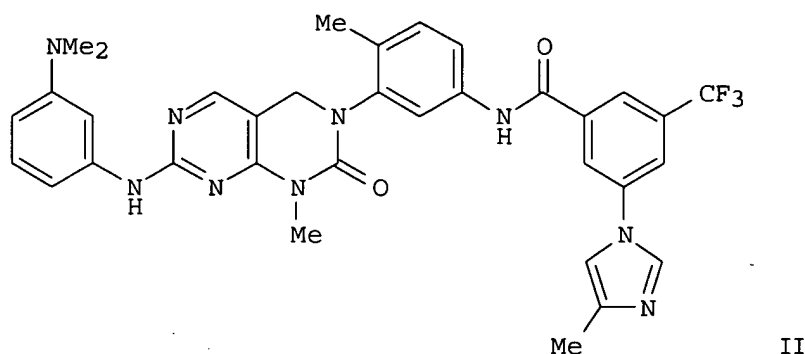
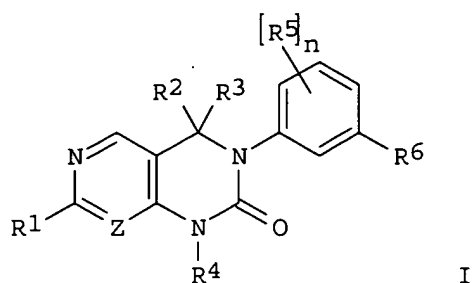
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2005011597 | A2 | 20050210 | WO 2004-US24764 | 20040729 |
| WO 2005011597 | A3 | 20050324 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: US 2003-491133P P 20030729

OTHER SOURCE(S): MARPAT 142:198094

GI



AB The invention provides a novel class of compds. I [$n = 0-4$; $Z = N, CH$; $R_1 = H, \text{alkyl, arylalkyl, hydroxy, alkoxy, etc.}$; $R_2, R_3 = H, \text{alkyl}$; or R_1 and R_2 together form O or S ; $R_4 = H, OH, NH_2, \text{alkyl, etc.}$; $R_5 = \text{alkyl, alkenyl, alkoxy, etc.}$; $R_6 = NR_{12}Y(O)R_{13}, Y(O)NR_{12}R_{13}$ (wherein $Y = C, P(O), S(O)$; $R_{12} = H, \text{alkyl}$; $R_{13} = \text{aryl, heteroaryl, cycloalkyl, etc.}$)], pharmaceutical compns. comprising such compds. and methods of using such compds. to treat or prevent diseases or disorders associated with abnormal or deregulated kinase activity, particularly diseases or disorders that involve abnormal activation of the Abl, BCR-Abl, Bmx, c-Raf, Csk, Fes, FGFR, Flt3, Ikk, IR, JNK, Lck, Mkk, PKC, PKD, Rsk, SAPK, Syk, Trk, BTK, Src, EGFR, IGF, Mek, Ros and Tie2 kinases. E.g., a multi-step synthesis of II, starting from 4-amino-2-methylsulfanylpurimidine-5-carbonitrile, was given. The compds. I show a percentage inhibition of greater than 50% against the mentioned above kinases at $10 \mu M$.

IT 839705-51-0P 839705-52-1P 839705-53-2P
 839705-54-3P 839705-55-4P 839705-56-5P
 839705-57-6P 839705-58-7P 839705-59-8P
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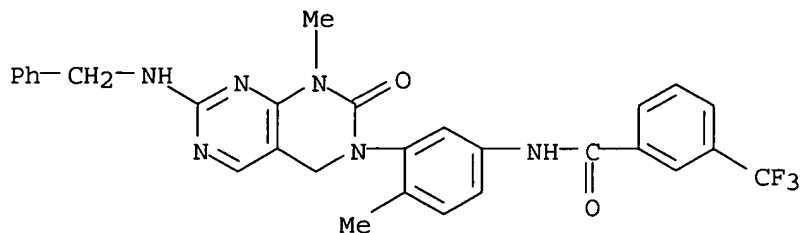
839708-02-0P 839708-03-1P 839708-08-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrimidopyrimidines as protein kinase inhibitors)

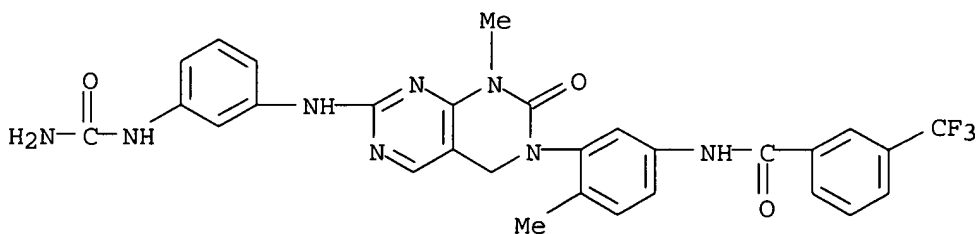
RN 839705-51-0 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-[(phenylmethyl)amino]pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



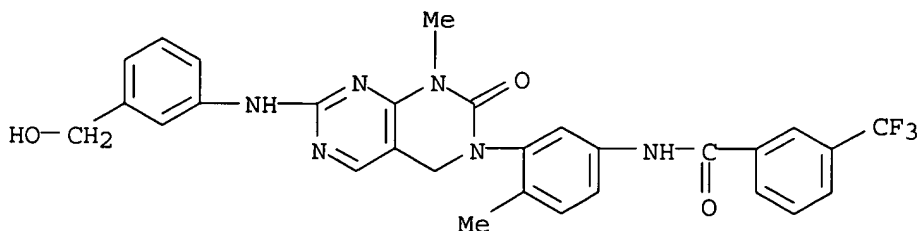
RN 839705-52-1 HCAPLUS

CN Benzamide, N-[3-[7-[[3-[(aminocarbonyl)amino]phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839705-53-2 HCAPLUS

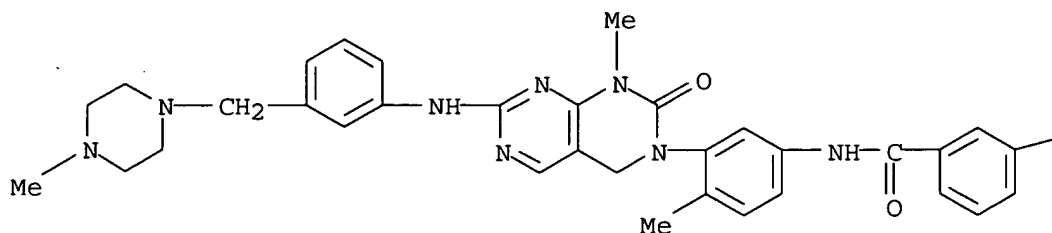
CN Benzamide, N-[3-[1,4-dihydro-7-[[3-(hydroxymethyl)phenyl]amino]-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839705-54-3 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[3-[(4-methyl-1-piperazinyl)methyl]phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

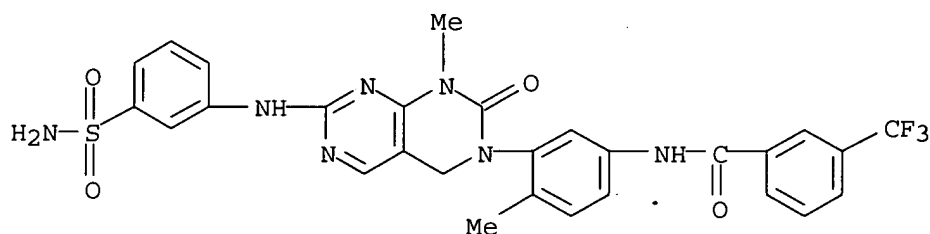


PAGE 1-B

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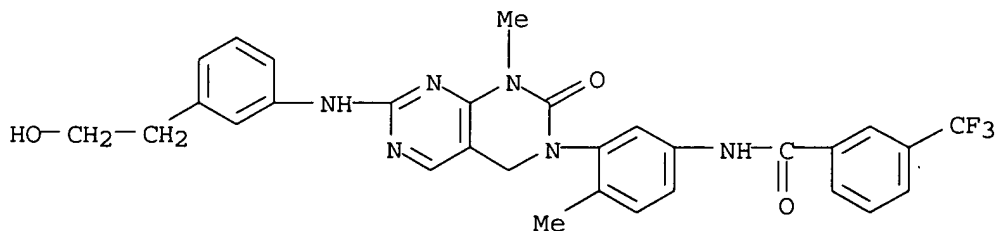
RN 839705-55-4 HCAPLUS

CN Benzamide, N-[3-[7-[[3-(aminosulfonyl)phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



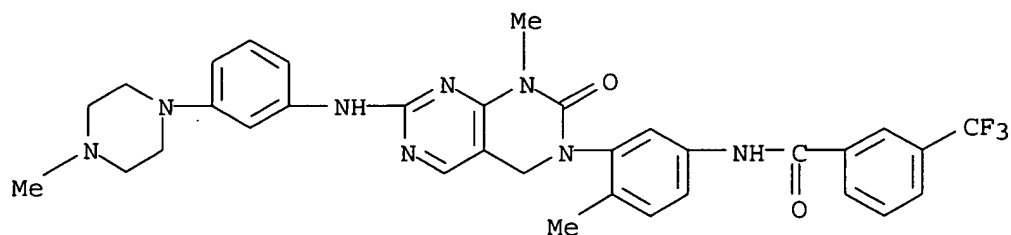
RN 839705-56-5 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-7-[[3-(2-hydroxyethyl)phenyl]amino]-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



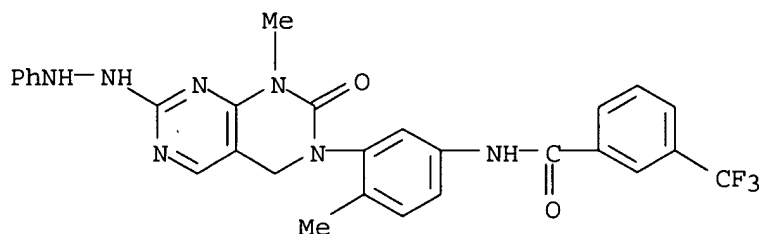
RN 839705-57-6 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[3-(4-methyl-1-piperazinyl)phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



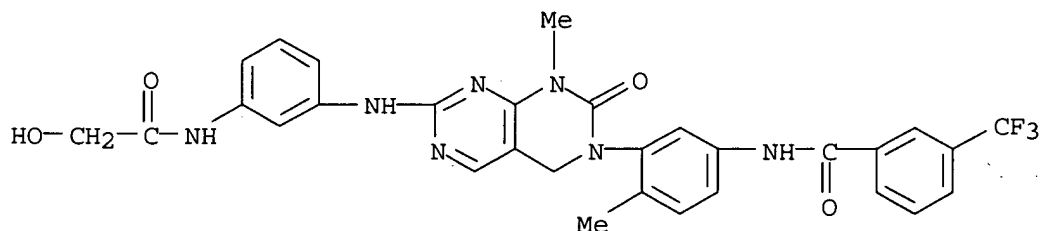
RN 839705-58-7 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-(2-phenylhydrazino)pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



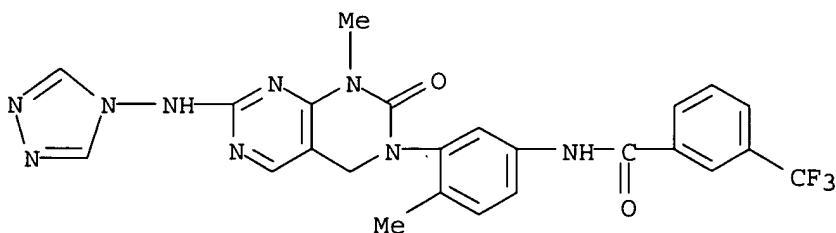
RN 839705-59-8 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-7-[[3-[(hydroxyacetyl)amino]phenyl]amino]-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



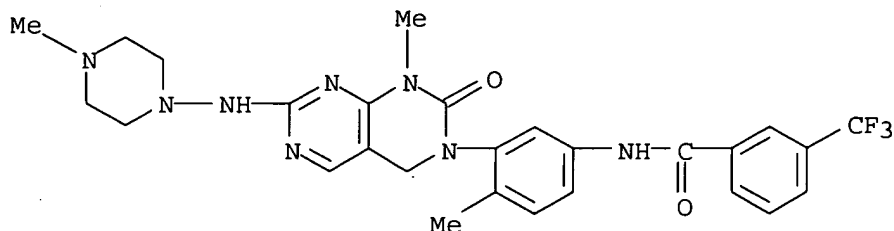
RN 839705-60-1 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-(4H-1,2,4-triazol-4-ylamino)pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



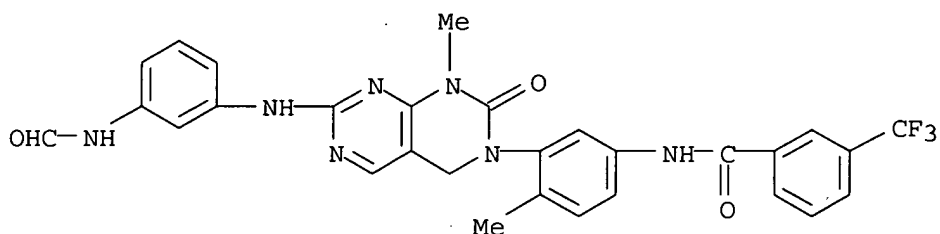
RN 839705-61-2 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[(4-methyl-1-piperazinyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



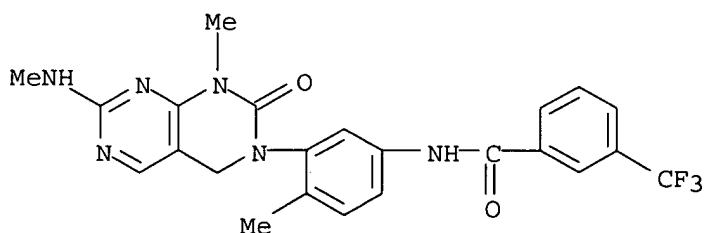
RN 839705-62-3 HCAPLUS

CN Benzamide, N-[3-[7-[[3-(formylamino)phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



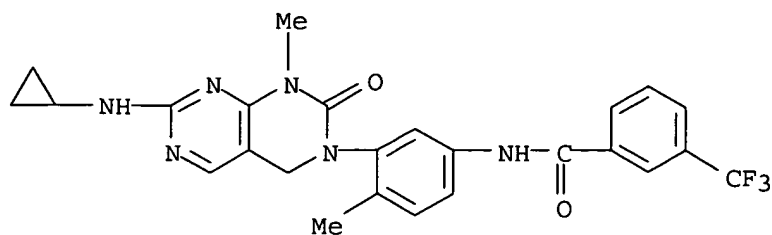
RN 839705-63-4 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



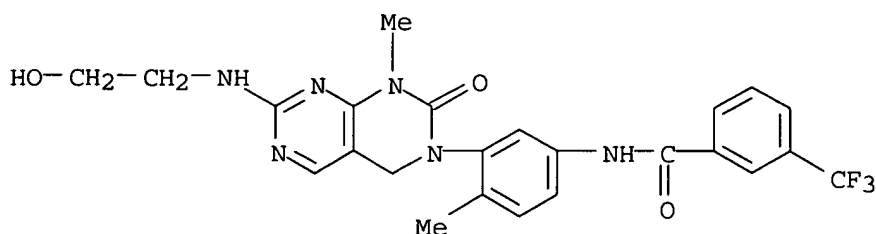
RN 839705-64-5 HCAPLUS

CN Benzamide, N-[3-[7-(cyclopropylamino)-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



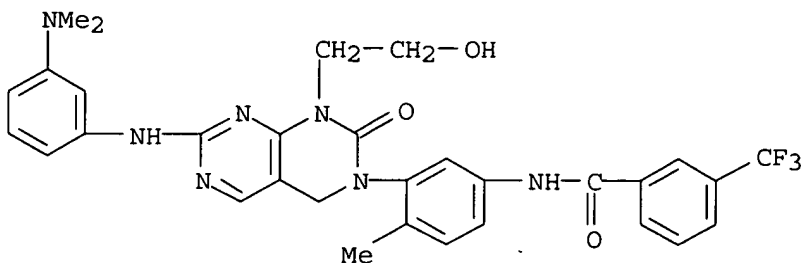
RN 839705-65-6 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-7-[(2-hydroxyethyl)amino]-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



RN 839705-66-7 HCAPLUS

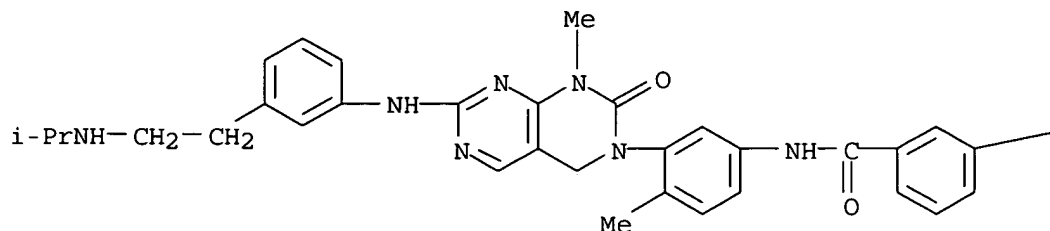
CN Benzamide, N-[3-[7-[[3-(dimethylamino)phenyl]amino]-1,4-dihydro-1-(2-hydroxyethyl)-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



RN 839705-67-8 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[3-[2-[(1-methylethyl)amino]ethyl]phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)

PAGE 1-A

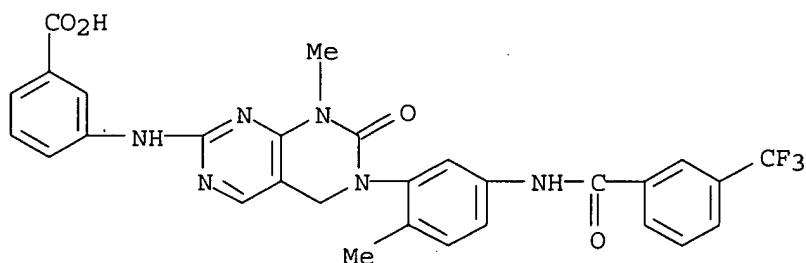


PAGE 1-B

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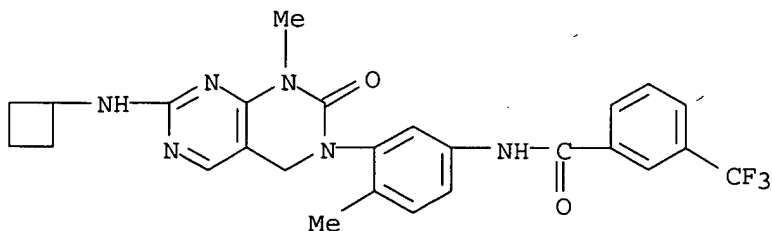
RN 839705-69-0 HCAPLUS

CN Benzoic acid, 3-[[5,6,7,8-tetrahydro-8-methyl-6-[2-methyl-5-[[3-(trifluoromethyl)benzoyl]amino]phenyl]-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]- (9CI) (CA INDEX NAME)



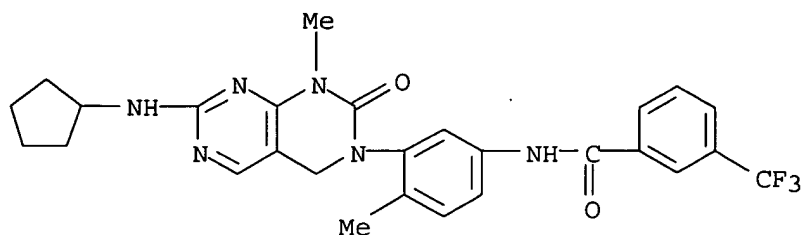
RN 839705-70-3 HCAPLUS

CN Benzamide, N-[3-[7-(cyclobutylamino)-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839705-71-4 HCAPLUS

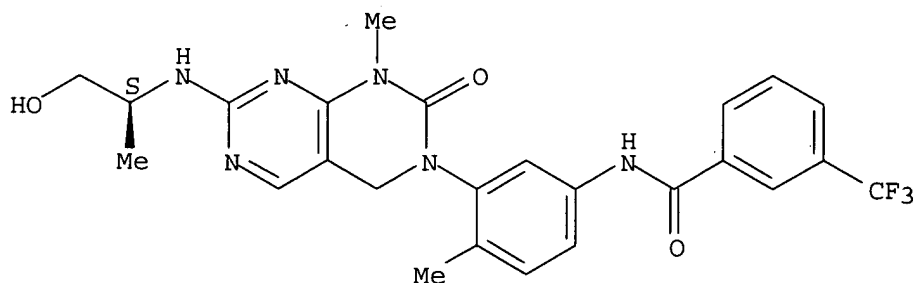
CN Benzamide, N-[3-[7-(cyclopentylamino)-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839705-72-5 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-7-[[(1S)-2-hydroxy-1-methylethyl]amino]-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

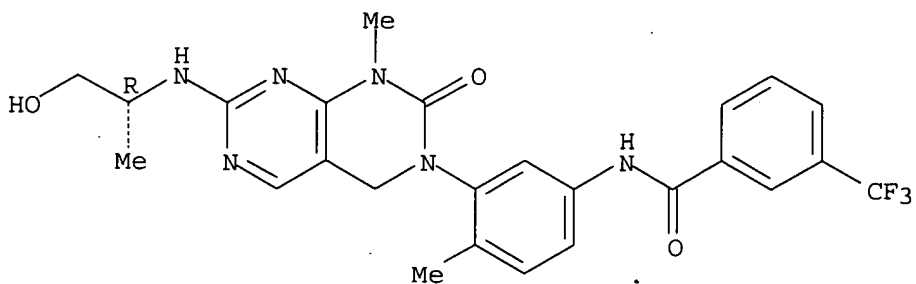
Absolute stereochemistry.



RN 839705-73-6 HCAPLUS

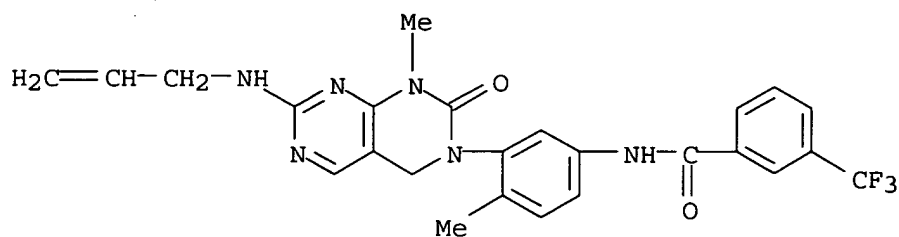
CN Benzamide, N-[3-[1,4-dihydro-7-[[(1R)-2-hydroxy-1-methylethyl]amino]-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



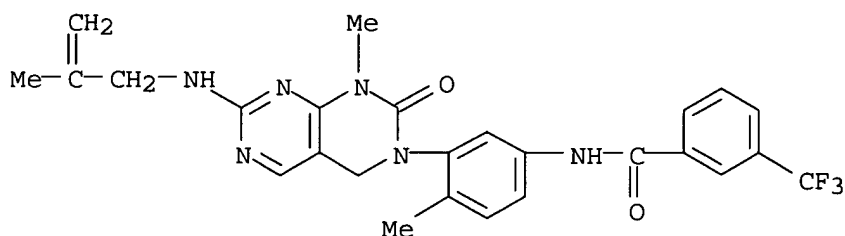
RN 839705-74-7 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-(2-propenylamino)pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



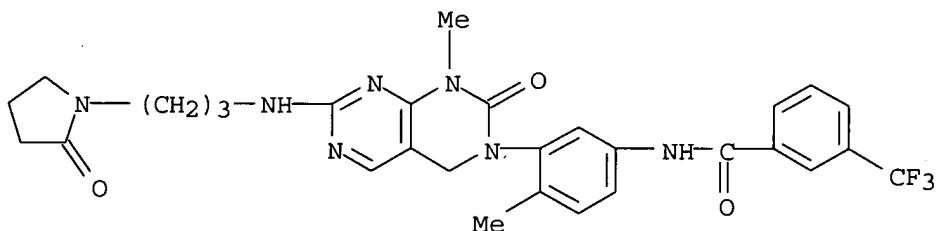
RN 839705-75-8 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[(2-methyl-2-propenyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



RN 839705-76-9 HCAPLUS

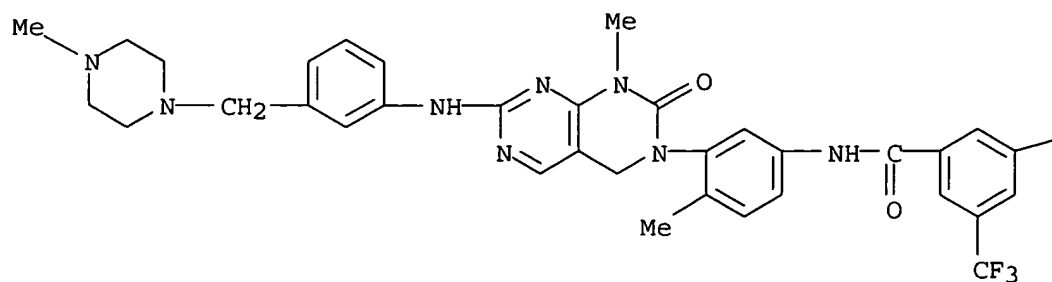
CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-[[3-(2-oxo-1-pyrrolidinyl)propyl]amino]pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



RN 839705-77-0 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[3-[(4-methyl-1-piperazinyl)methyl]phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(dimethylamino)-5-(trifluoromethyl)-(9CI) (CA INDEX NAME)

PAGE 1-A

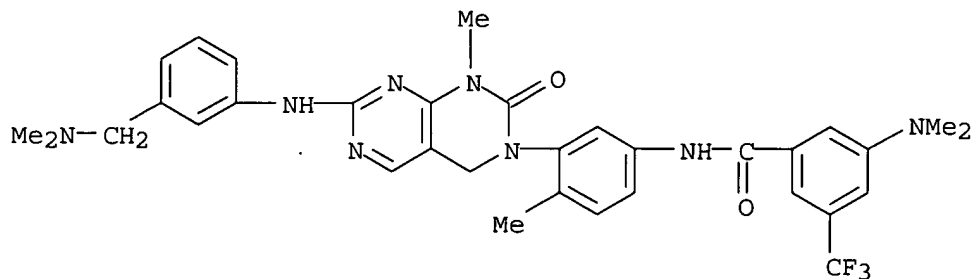


PAGE 1-B

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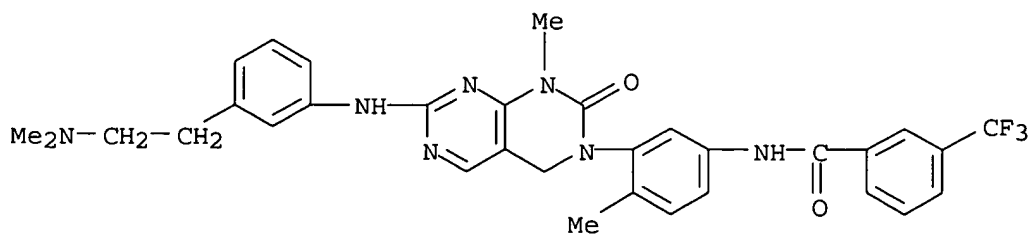
RN 839705-78-1 HCAPLUS

CN Benzamide, 3-(dimethylamino)-N-[3-[7-[[3-[(dimethylamino)methyl]phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839705-79-2 HCAPLUS

CN Benzamide, N-[3-[7-[[3-[2-(dimethylamino)ethyl]phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

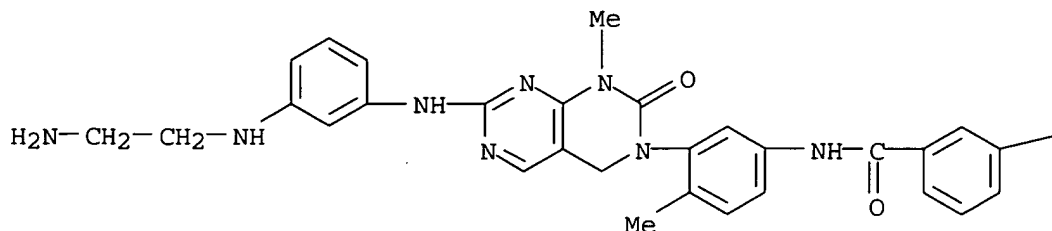


RN 839705-80-5 HCAPLUS

CN Benzamide, N-[3-[7-[[3-[(2-aminoethyl)amino]phenyl]amino]-1,4-dihydro-1-

methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

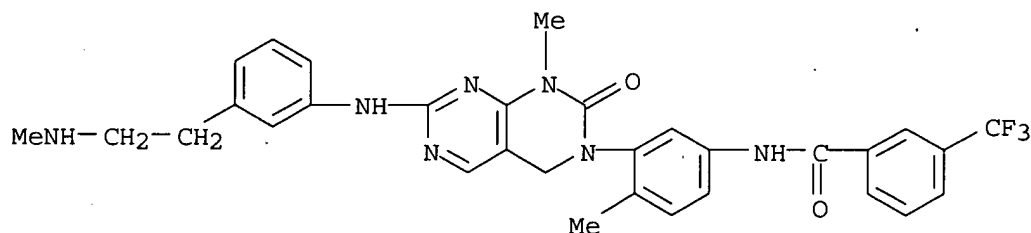


PAGE 1-B

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RN 839705-81-6 HCAPLUS

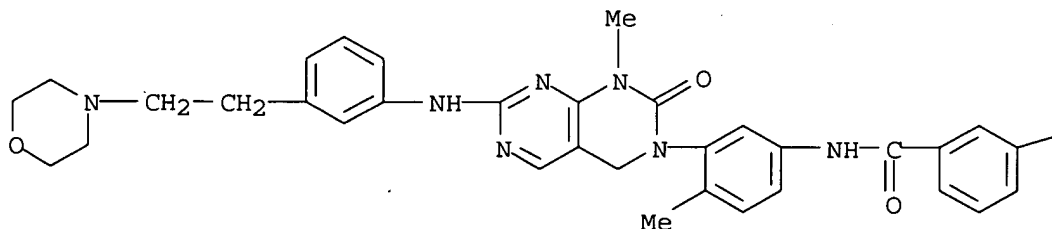
CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[3-[2-(methylamino)ethyl]phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839705-82-7 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[3-[2-(4-morpholinyl)ethyl]phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

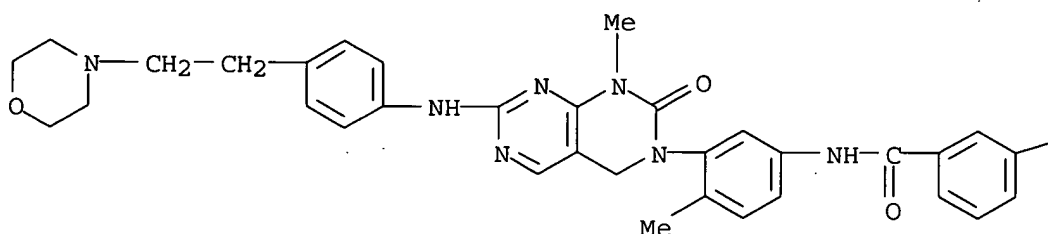


PAGE 1-B

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RN 839705-83-8 HCAPLUS
 CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[4-[2-(4-morpholinyl)ethyl]phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

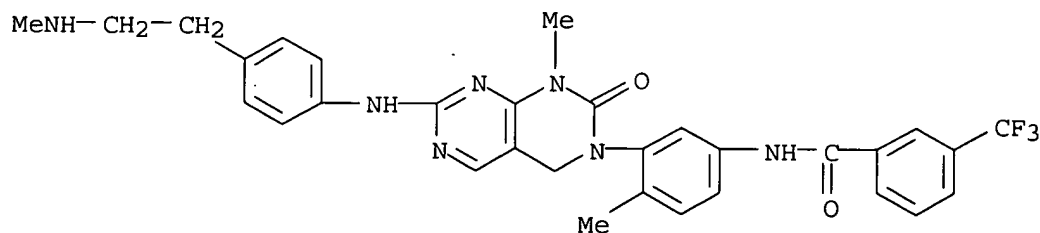
PAGE 1-A



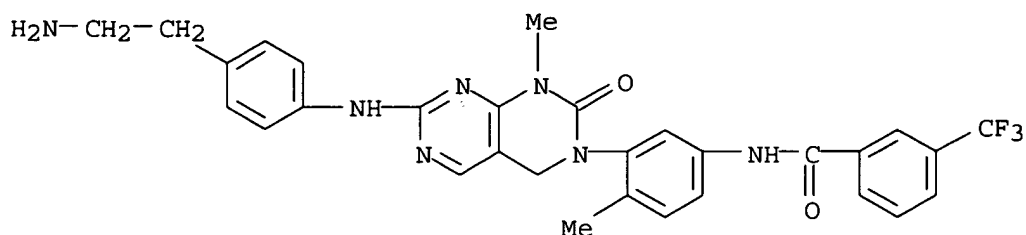
PAGE 1-B

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RN 839705-84-9 HCAPLUS
 CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[4-[2-(methylamino)ethyl]phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

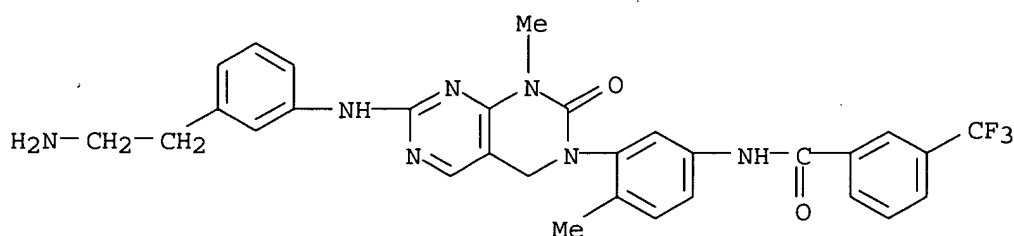


RN 839705-85-0 HCAPLUS
 CN Benzamide, N-[3-[7-[[4-(2-aminoethyl)phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



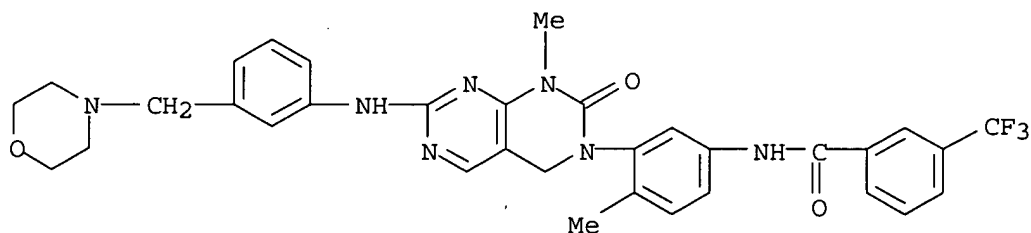
RN 839705-86-1 HCAPLUS

CN Benzamide, N-[3-[7-[[3-(2-aminoethyl)phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



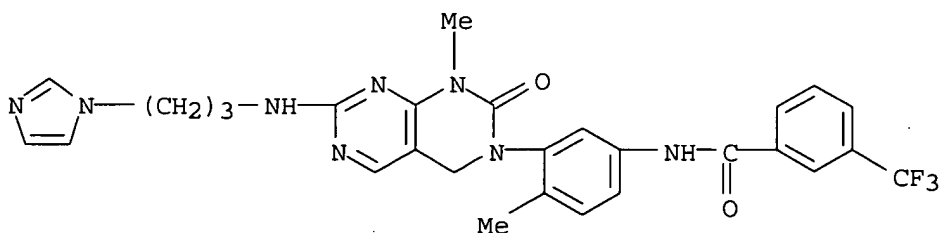
RN 839705-87-2 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[3-(4-morpholinylmethyl)phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



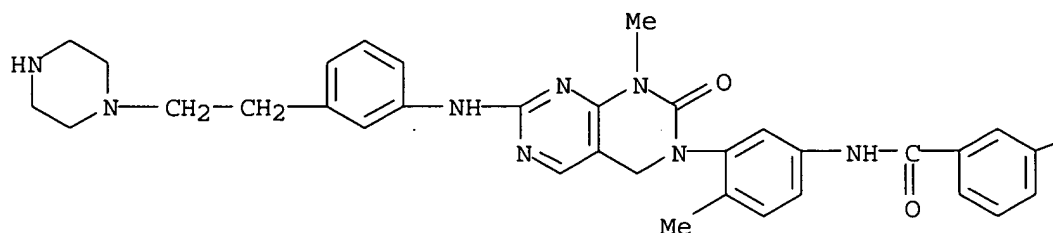
RN 839705-88-3 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-7-[[3-(1H-imidazol-1-yl)propyl]amino]-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



RN 839705-89-4 HCAPLUS
 CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-[[3-[2-(1-piperazinyl)ethyl]phenyl]amino]pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

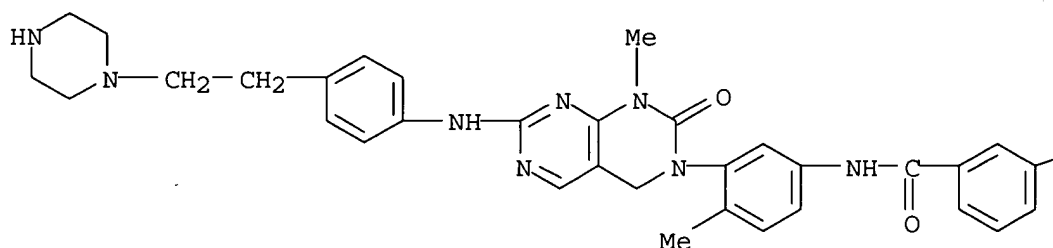


PAGE 1-B

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RN 839705-90-7 HCAPLUS
 CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-[[4-[2-(1-piperazinyl)ethyl]phenyl]amino]pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

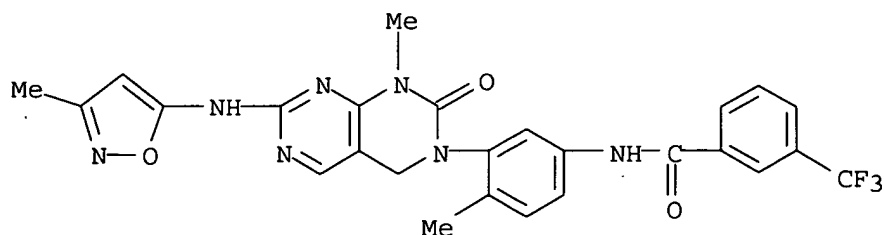
PAGE 1-A



PAGE 1-B

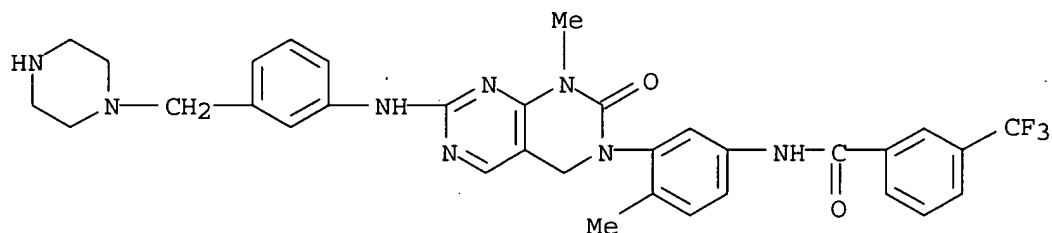
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RN 839705-91-8 HCAPLUS
 CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[(3-methyl-5-isoxazolyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



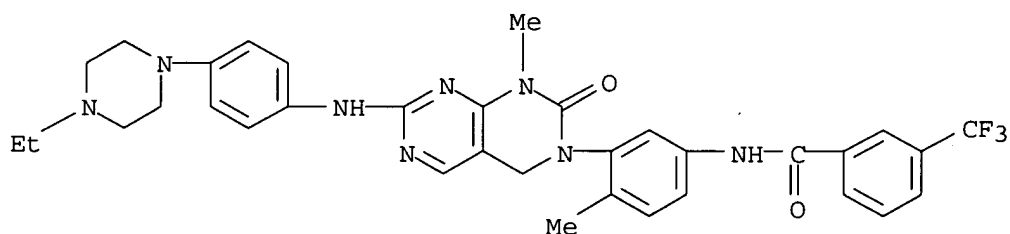
RN 839705-92-9 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-[[3-(1-piperazinylmethyl)phenyl]amino]pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



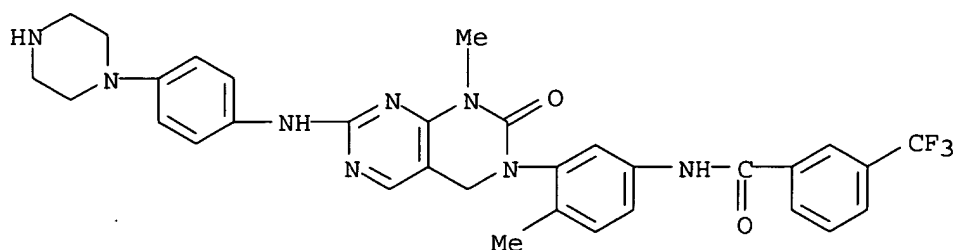
RN 839705-93-0 HCAPLUS

CN Benzamide, N-[3-[7-[[4-(4-ethyl-1-piperazinyl)phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



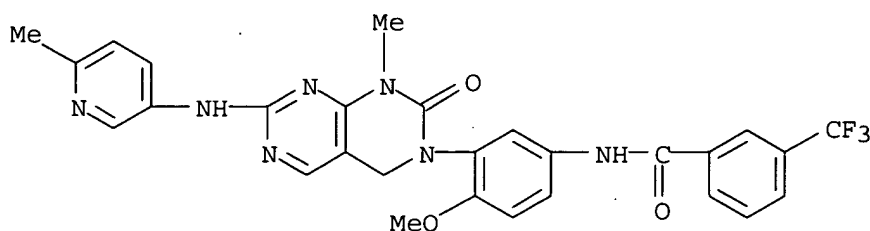
RN 839705-94-1 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-[[4-(1-piperazinyl)phenyl]amino]pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



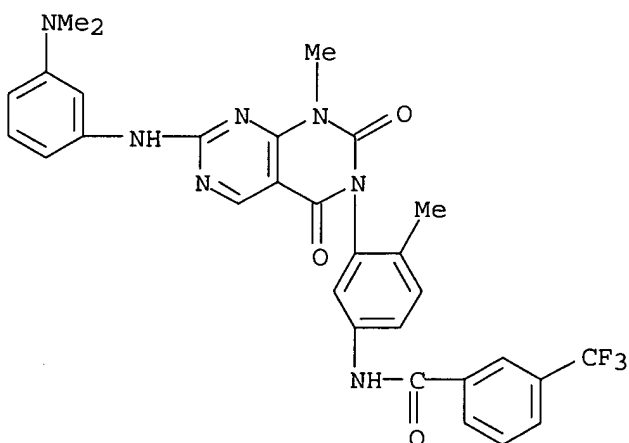
RN 839705-95-2 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[(6-methyl-3-pyridinyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methoxyphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



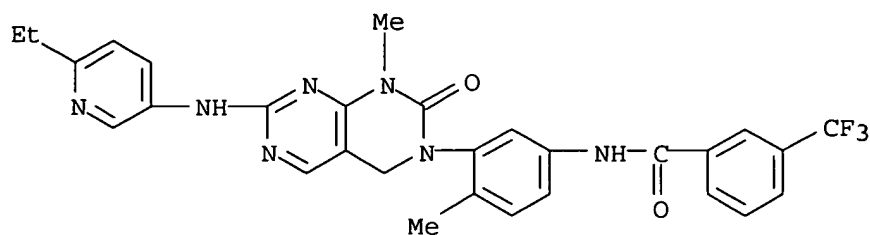
RN 839705-97-4 HCAPLUS

CN Benzamide, N-[3-[7-[[3-(dimethylamino)phenyl]amino]-1,4-dihydro-1-methyl-2,4-dioxypyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



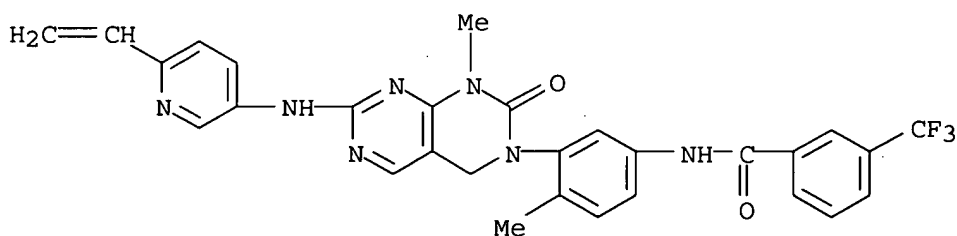
RN 839705-98-5 HCAPLUS

CN Benzamide, N-[3-[7-[(6-ethyl-3-pyridinyl)amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



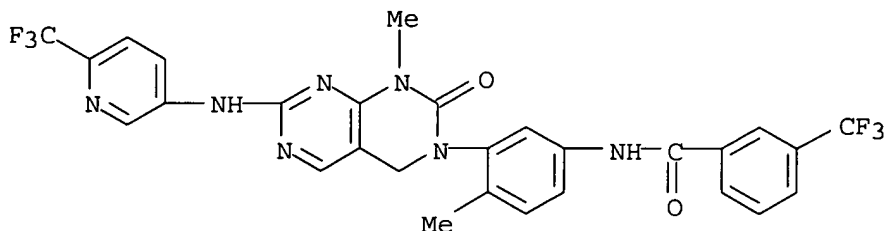
RN 839705-99-6 HCAPLUS

CN Benzamide, N-[3-[7-[(6-ethenyl-3-pyridinyl)amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



RN 839706-00-2 HCAPLUS

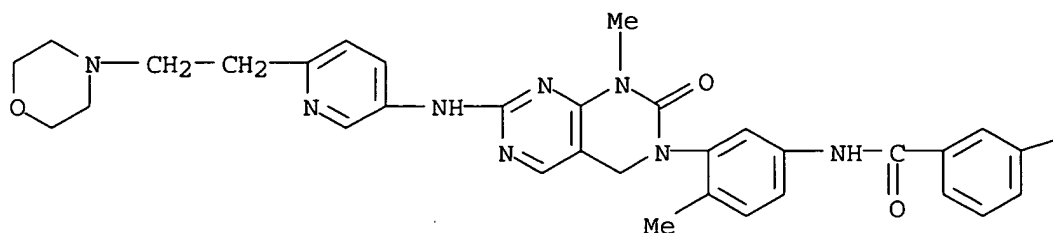
CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-[(6-(trifluoromethyl)-3-pyridinyl)amino]pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



RN 839706-01-3 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[6-[2-(4-morpholinyl)ethyl]-3-pyridinyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)

PAGE 1-A

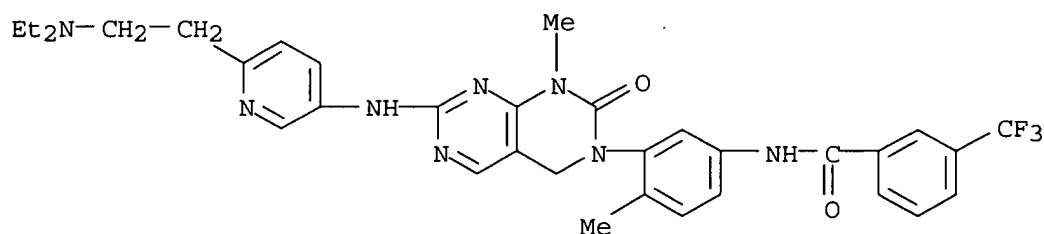


PAGE 1-B

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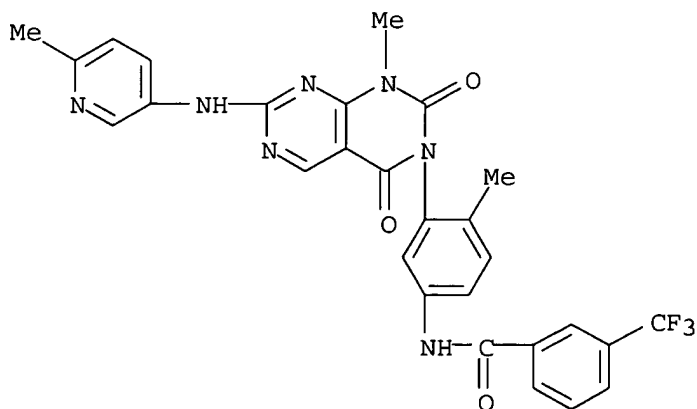
RN 839706-02-4 HCAPLUS

CN Benzamide, N-[3-[7-[[6-[2-(diethylamino)ethyl]-3-pyridinyl]amino]-1,4-dihydro-1-methyl-2-oxypyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



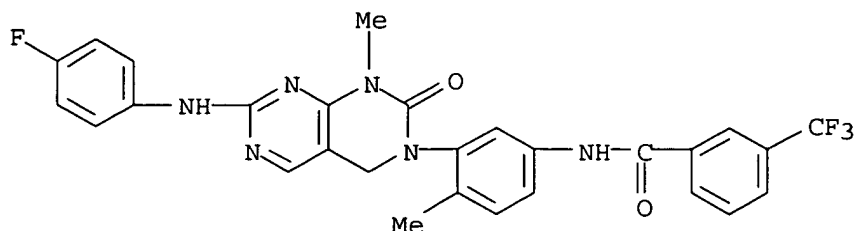
RN 839706-03-5 HCAPLUS

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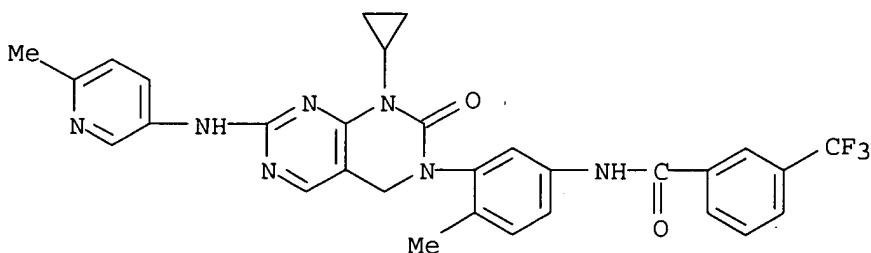
RN 839706-04-6 HCAPLUS

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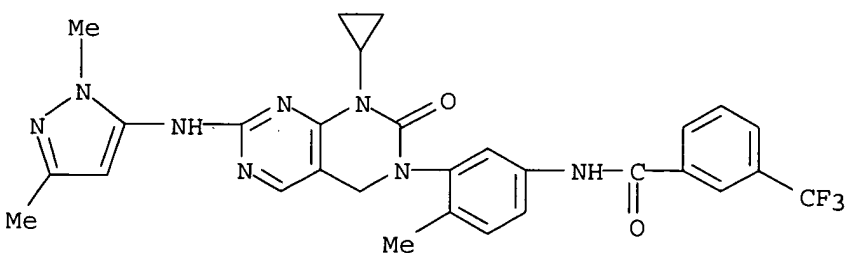
RN 839706-05-7 HCAPLUS

CN Benzamide, N-[3-[1-cyclopropyl-1,4-dihydro-7-[(6-methyl-3-pyridinyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



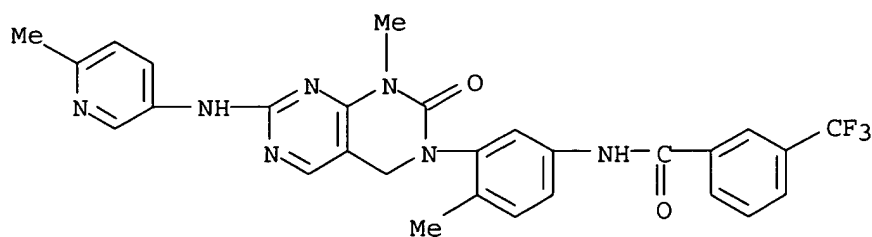
RN 839706-06-8 HCAPLUS

CN Benzamide, N-[3-[1-cyclopropyl-7-[(1,3-dimethyl-1H-pyrazol-5-yl)amino]-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



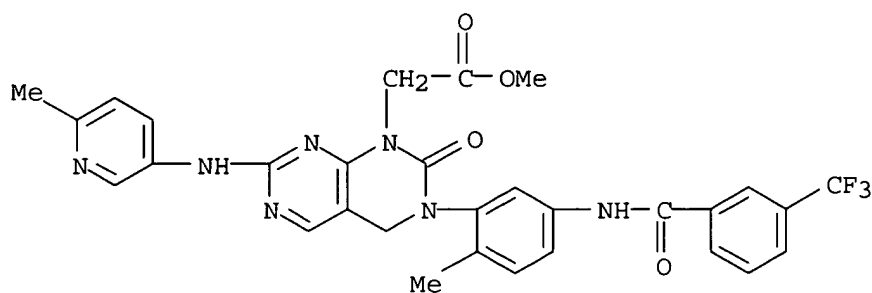
RN 839706-07-9 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[(6-methyl-3-pyridinyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



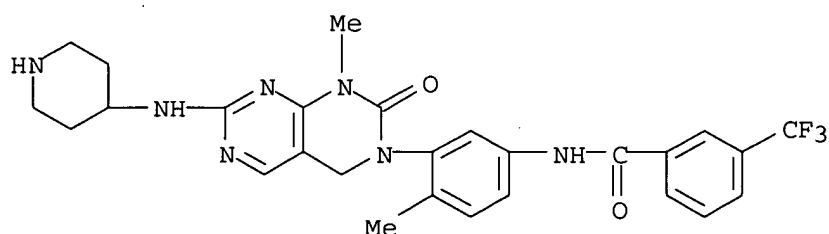
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CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetic acid, 3,4-dihydro-7-[(6-methyl-3-pyridinyl)amino]-3-[2-methyl-5-[[3-(trifluoromethyl)benzoyl]amino]phenyl]-2-oxo-, methyl ester (9CI) (CA INDEX NAME)



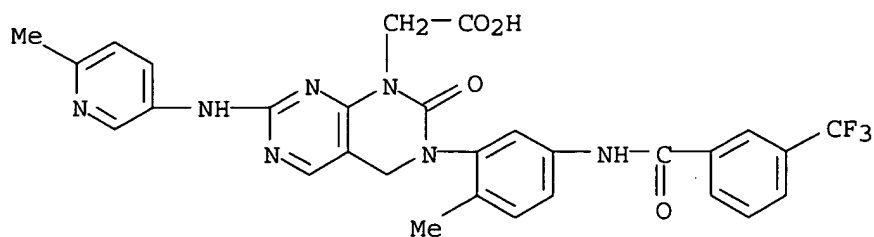
RN 839706-09-1 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-(4-piperidinylamino)pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



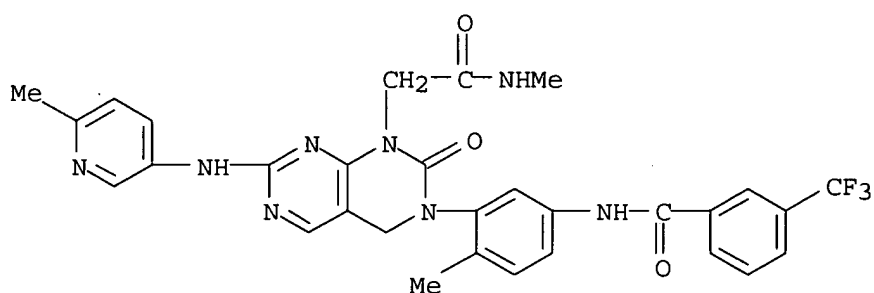
RN 839706-10-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetic acid, 3,4-dihydro-7-[(6-methyl-3-pyridinyl)amino]-3-[2-methyl-5-[[3-(trifluoromethyl)benzoyl]amino]phenyl]-2-oxo- (9CI) (CA INDEX NAME)



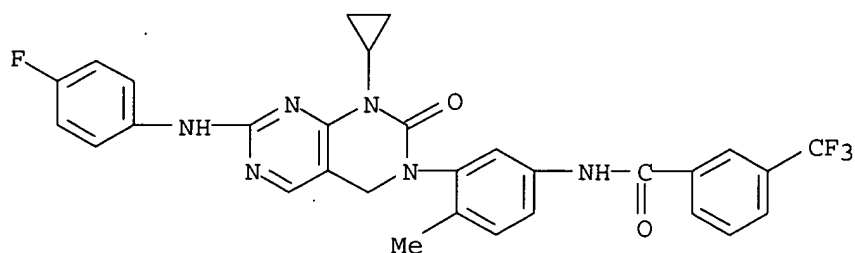
RN 839706-11-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetamide, 3,4-dihydro-N-methyl-7-[(6-methyl-3-pyridinyl)amino]-3-[2-methyl-5-[3-(trifluoromethyl)benzoyl]amino]phenyl]-2-oxo- (9CI) (CA INDEX NAME)



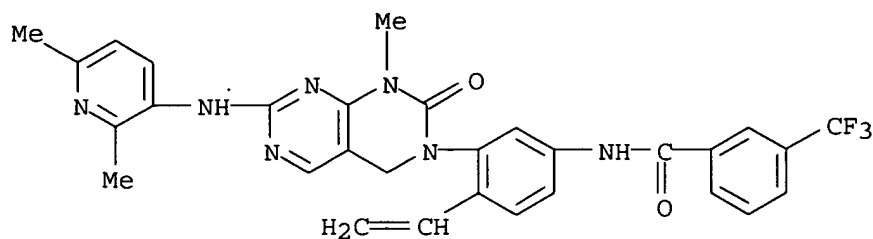
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CN Benzamide, N-[3-[1-cyclopropyl-7-[(4-fluorophenyl)amino]-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



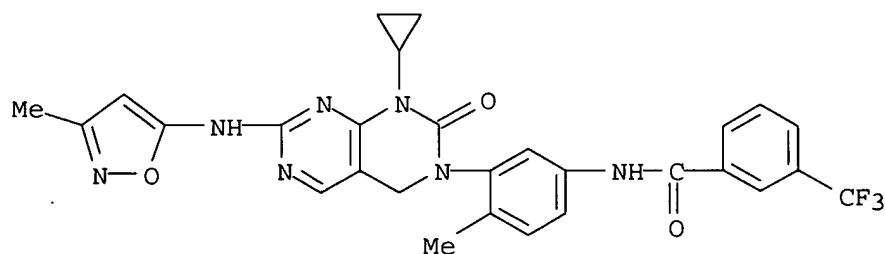
RN 839706-13-7 HCAPLUS

CN Benzamide, N-[3-[7-[(2,6-dimethyl-3-pyridinyl)amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-ethenylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



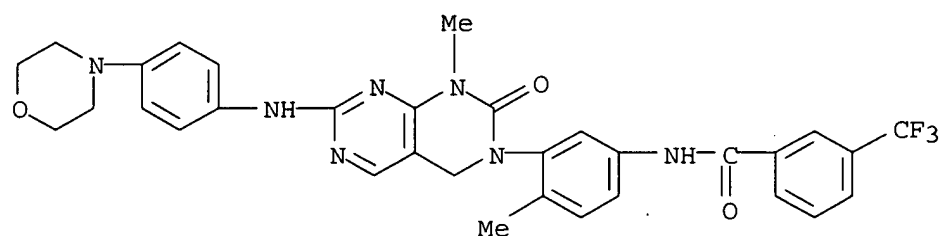
RN 839706-14-8 HCAPLUS

CN Benzamide, N-[3-[1-cyclopropyl-1,4-dihydro-7-[(3-methyl-5-isoxazolyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839706-15-9 HCAPLUS

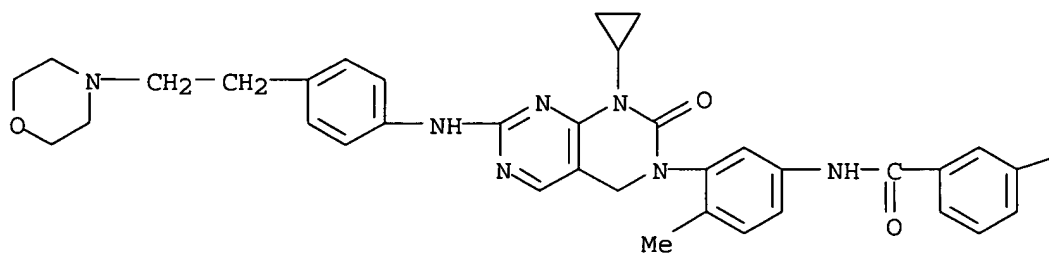
CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[4-(4-morpholinyl)phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839706-16-0 HCAPLUS

CN Benzamide, N-[3-[1-cyclopropyl-1,4-dihydro-7-[[4-[2-(4-morpholinyl)ethyl]phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

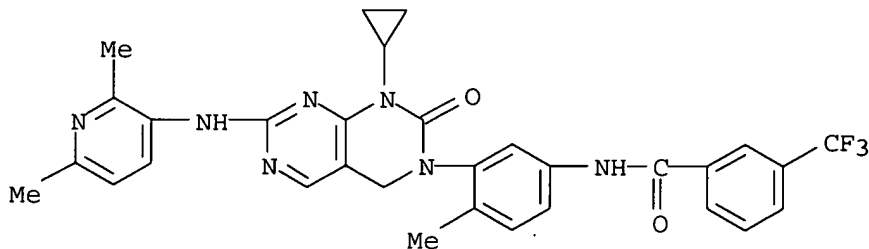


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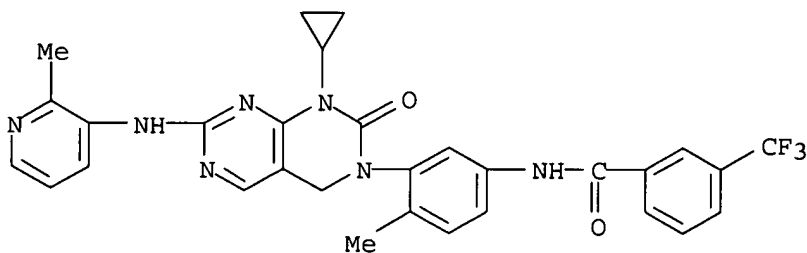
RN 839706-17-1 HCAPLUS

CN Benzamide, N-[3-[1-cyclopropyl-7-[(2,6-dimethyl-3-pyridinyl)amino]-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839706-18-2 HCAPLUS

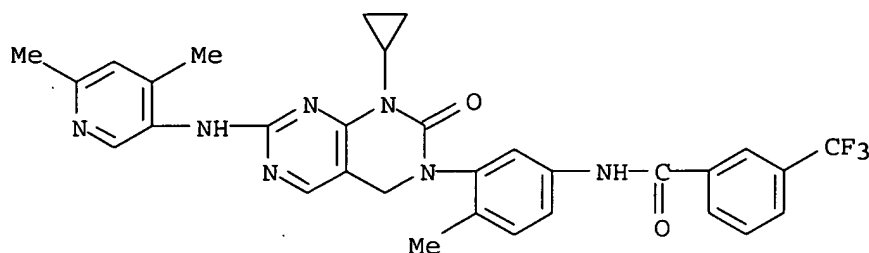
CN Benzamide, N-[3-[1-cyclopropyl-1,4-dihydro-7-[(2-methyl-3-pyridinyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839706-19-3 HCAPLUS

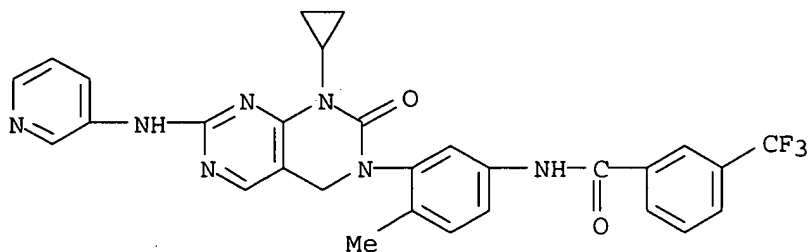
CN Benzamide, N-[3-[1-cyclopropyl-7-[(4,6-dimethyl-3-pyridinyl)amino]-1,4-

dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



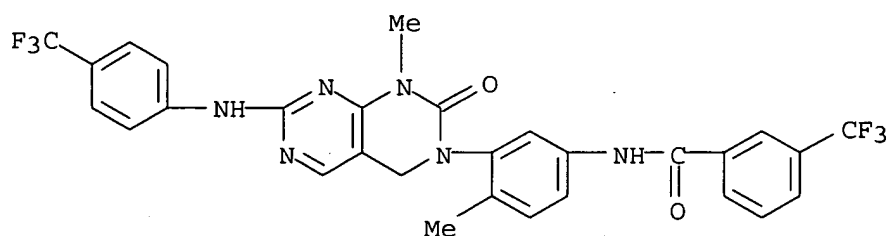
RN 839706-20-6 HCAPLUS

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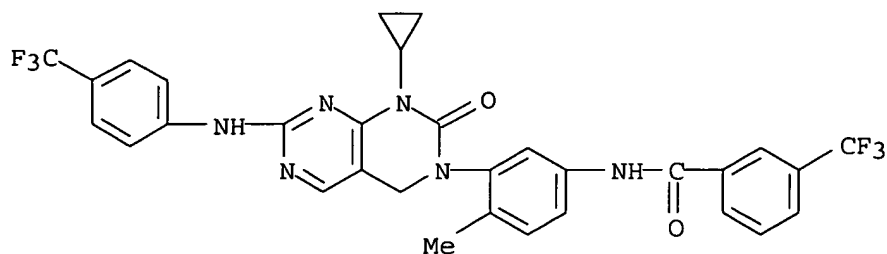
RN 839706-21-7 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-[[4-(trifluoromethyl)phenyl]amino]pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



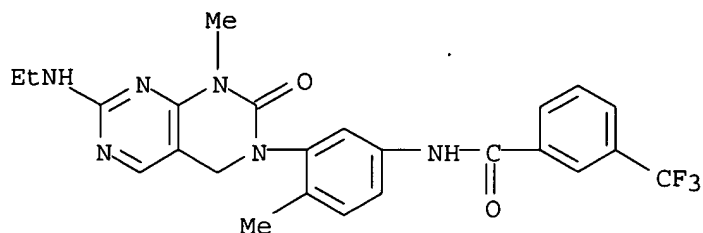
RN 839706-22-8 HCAPLUS

CN Benzamide, N-[3-[1-cyclopropyl-1,4-dihydro-2-oxo-7-[[4-(trifluoromethyl)phenyl]amino]pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



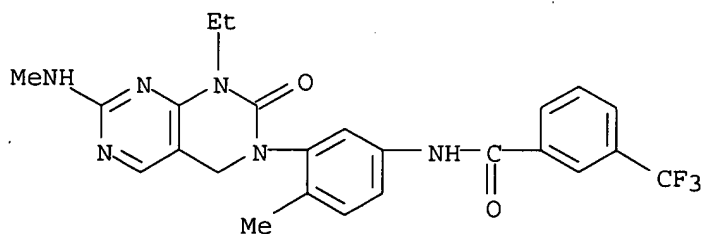
RN 839706-23-9 HCAPLUS

CN Benzamide, N-[3-[7-(ethylamino)-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



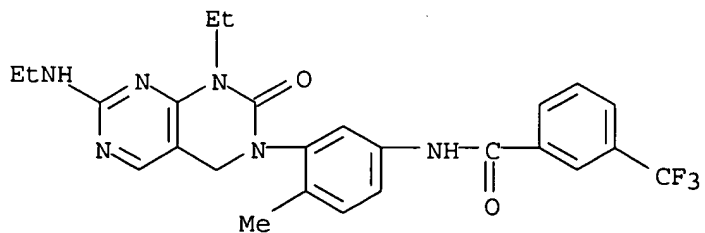
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CN Benzamide, N-[3-[1-ethyl-1,4-dihydro-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



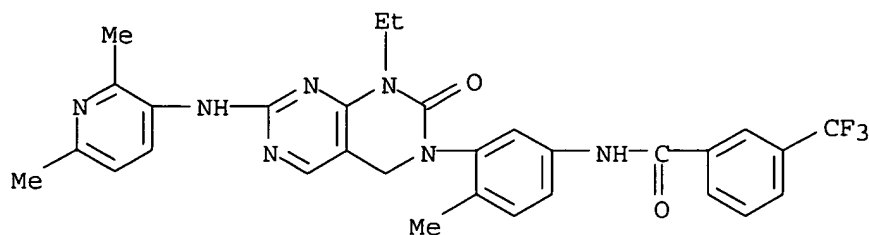
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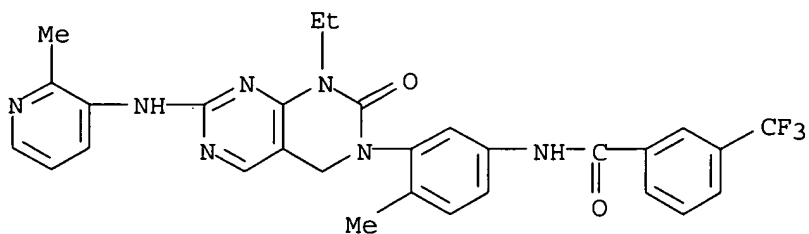
RN 839706-26-2 HCAPLUS

CN Benzamide, N-[3-[7-[(2,6-dimethyl-3-pyridinyl)amino]-1-ethyl-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



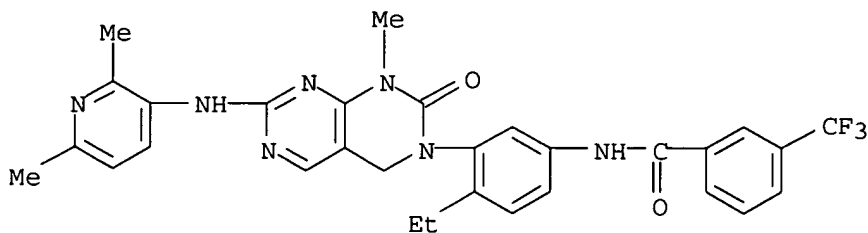
RN 839706-27-3 HCAPLUS

CN Benzamide, N-[3-[1-ethyl-1,4-dihydro-7-[(2-methyl-3-pyridinyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



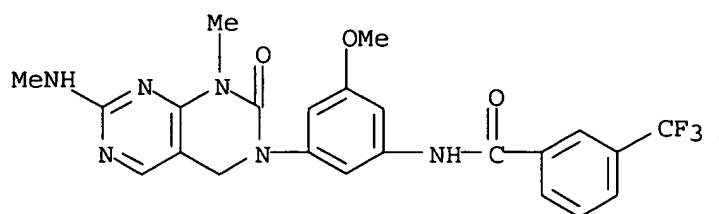
RN 839706-28-4 HCAPLUS

CN Benzamide, N-[3-[7-[(2,6-dimethyl-3-pyridinyl)amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-ethylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



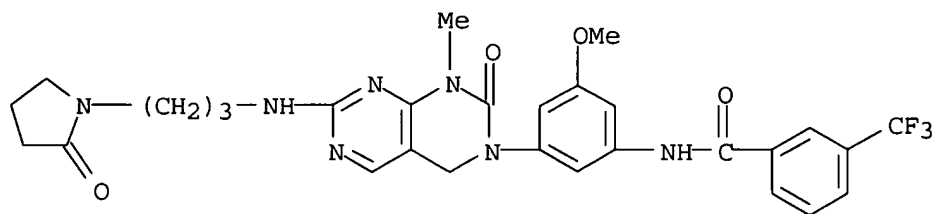
RN 839706-29-5 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



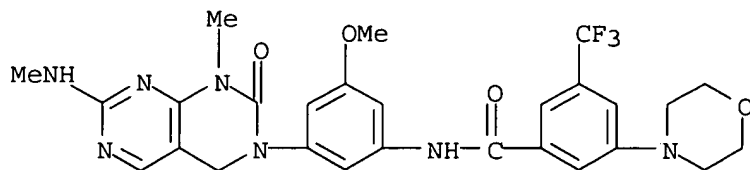
RN 839706-30-8 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-[[3-(2-oxo-1-pyrrolidinyl)propyl]amino]pyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



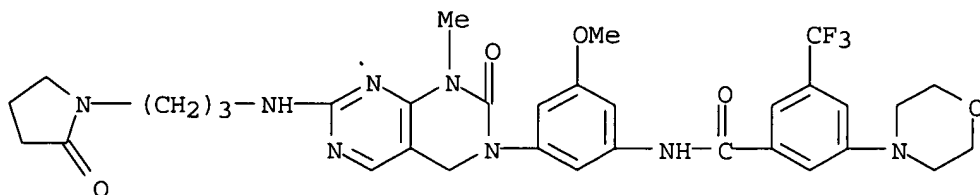
RN 839706-31-9 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(4-morpholinyl)-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839706-32-0 HCAPLUS

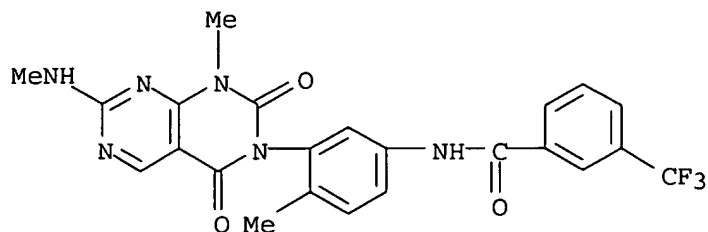
CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-[[3-(2-oxo-1-pyrrolidinyl)propyl]amino]pyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(4-morpholinyl)-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839706-33-1 HCAPLUS

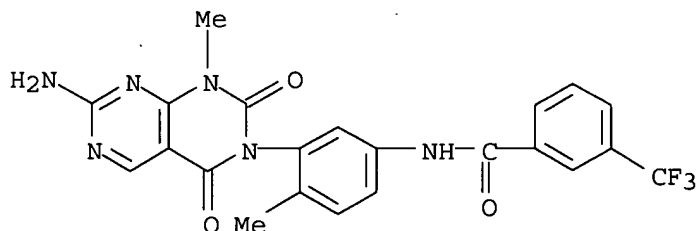
CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-(methylamino)-2,4-

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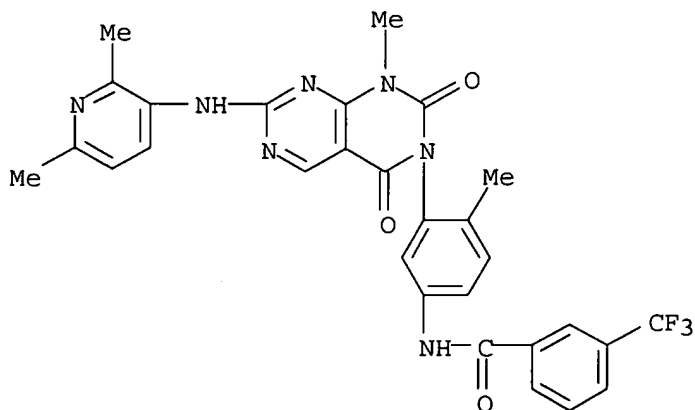
RN 839706-34-2 HCAPLUS

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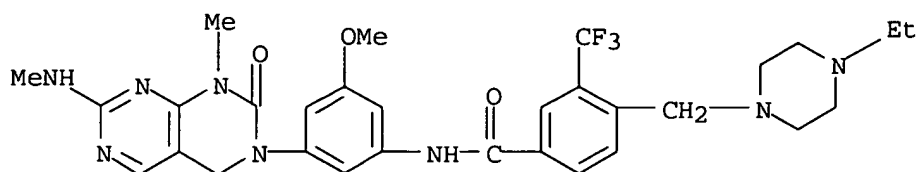
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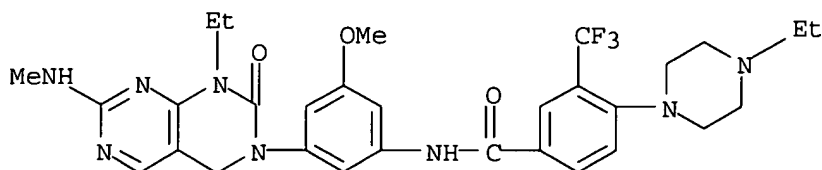
RN 839706-36-4 HCAPLUS

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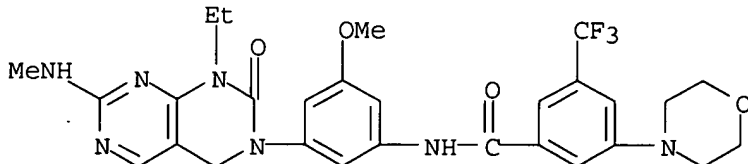
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CN Benzamide, N-[3-[1-ethyl-1,4-dihydro-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-4-(4-ethyl-1-piperazinyl)-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



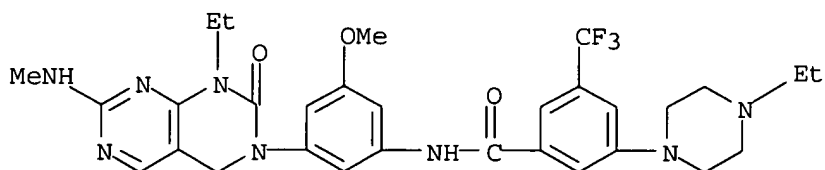
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CN Benzamide, N-[3-[1-ethyl-1,4-dihydro-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(4-morpholinyl)-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)



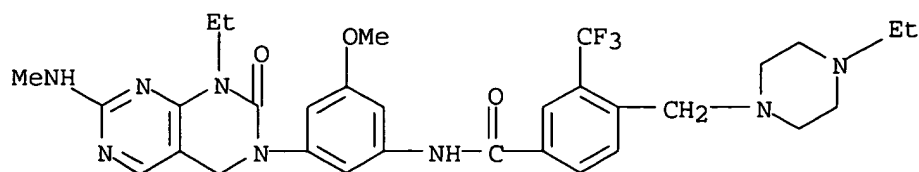
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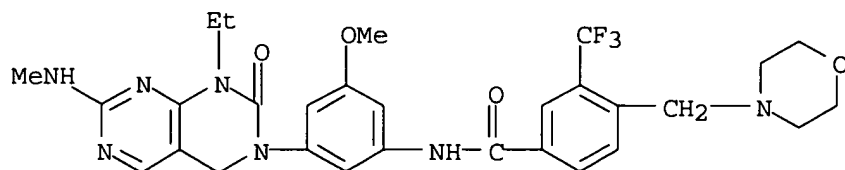
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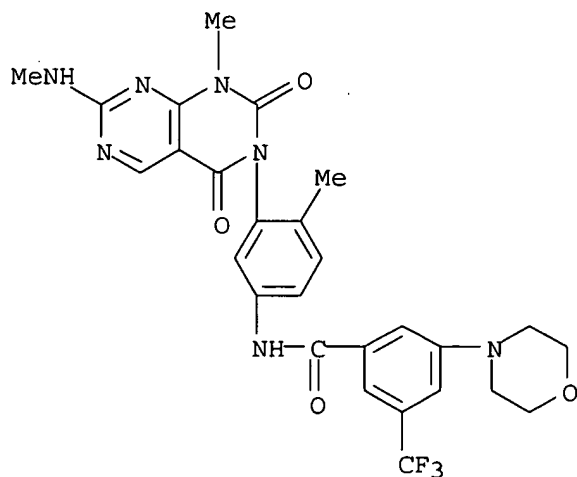
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CN Benzamide, N-[3-[1-ethyl-1,4-dihydro-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-4-(4-morpholinylmethyl)-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



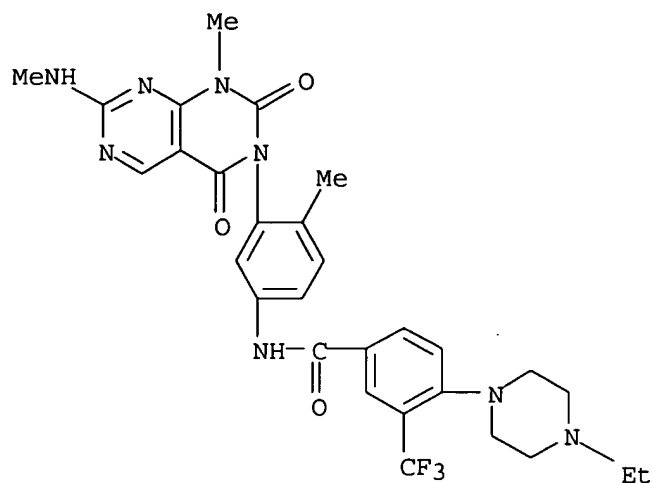
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CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-(methylamino)-2,4-dioxypyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(4-morpholinyl)-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)



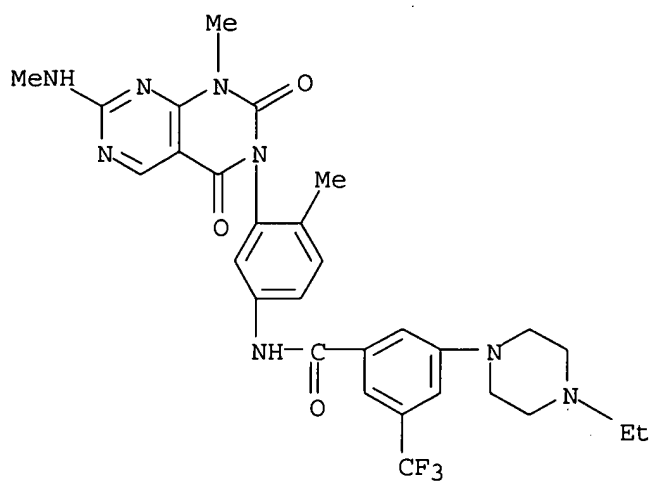
RN 839706-43-3 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-(methylamino)-2,4-dioxypyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-4-(4-ethyl-1-piperazinyl)-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



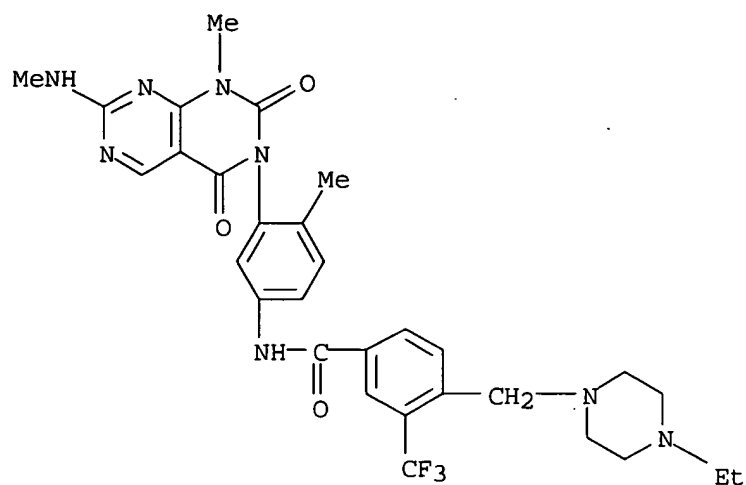
RN 839706-44-4 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-(methylamino)-2,4-dioxypyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(4-ethyl-1-piperazinyl)-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)



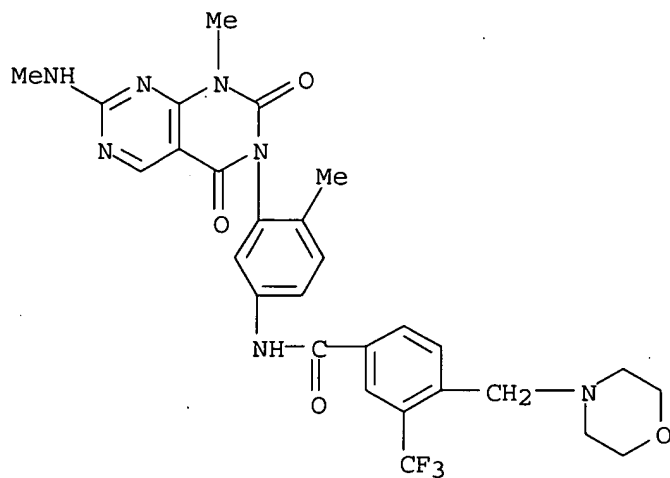
RN 839706-45-5 HCAPLUS

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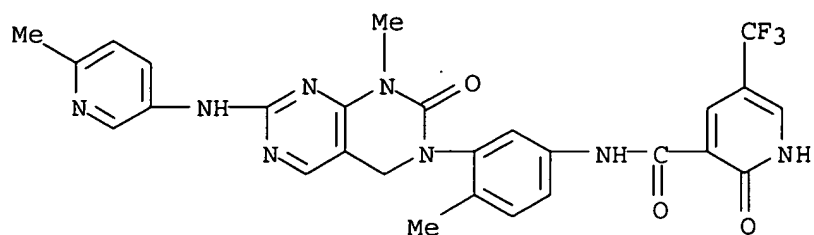
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CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-(methylamino)-2,4-dioxypyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-4-(4-morpholinylmethyl)-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



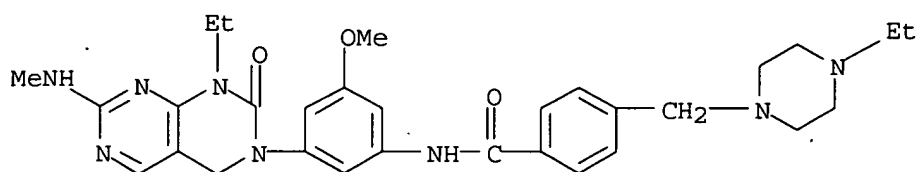
RN 839706-47-7 HCAPLUS

CN 3-Pyridinecarboxamide, N-[3-[1,4-dihydro-1-methyl-7-[(6-methyl-3-pyridinyl)amino]-2-oxypyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-1,2-dihydro-2-oxo-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)



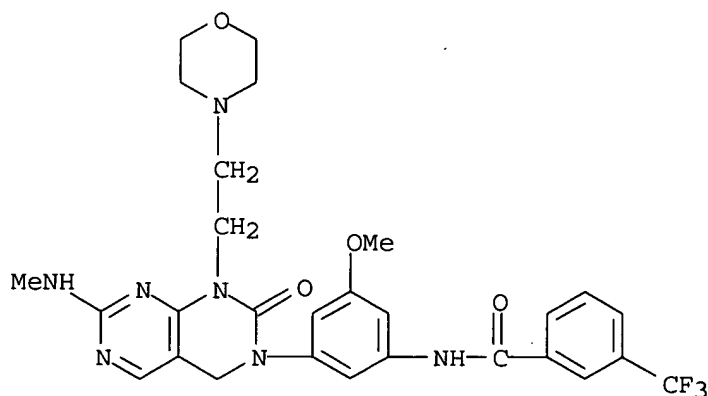
RN 839706-48-8 HCAPLUS

CN Benzamide, N-[3-[1-ethyl-1,4-dihydro-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-4-[(4-ethyl-1-piperazinyl)methyl]-
(9CI) (CA INDEX NAME)



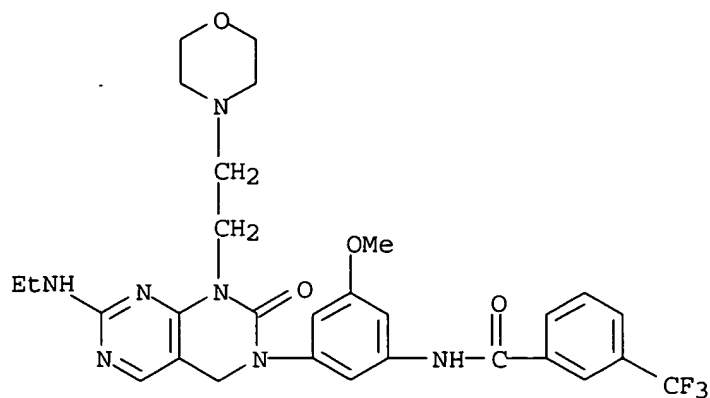
RN 839706-49-9 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-7-(methylamino)-1-[2-(4-morpholinyl)ethyl]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)-
(9CI) (CA INDEX NAME)



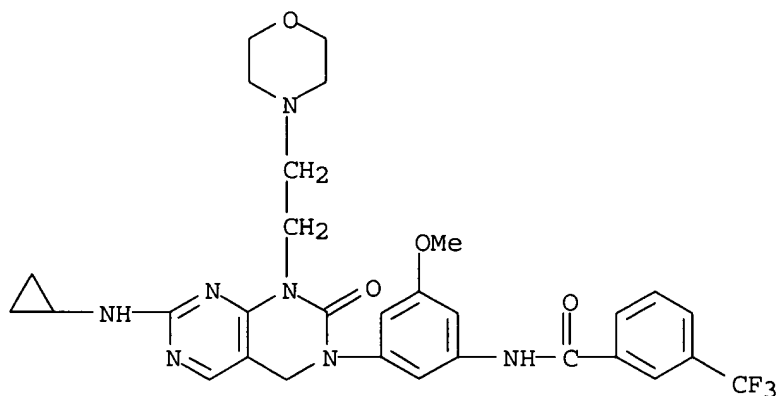
RN 839706-50-2 HCAPLUS

CN Benzamide, N-[3-[7-(ethylamino)-1,4-dihydro-1-[2-(4-morpholinyl)ethyl]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)-
(9CI) (CA INDEX NAME)



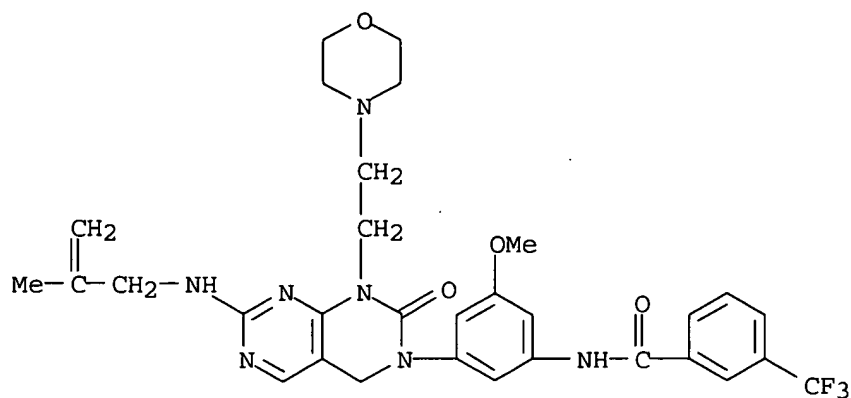
RN 839706-51-3 HCAPLUS

CN Benzamide, N-[3-[7-(cyclopropylamino)-1,4-dihydro-1-[2-(4-morpholinyl)ethyl]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



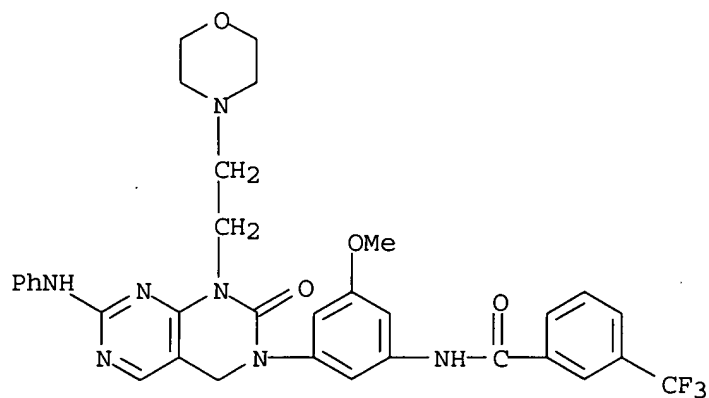
RN 839706-52-4 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-7-[(2-methyl-2-propenyl)amino]-1-[2-(4-morpholinyl)ethyl]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839706-53-5 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-[2-(4-morpholinyl)ethyl]-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

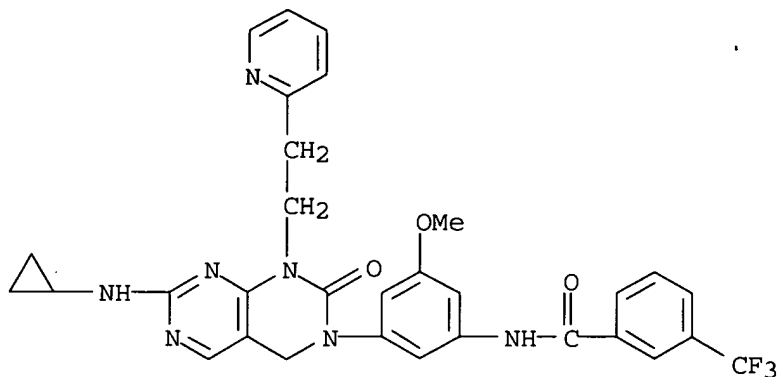


RN 839706-54-6 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-[2-(4-morpholinyl)ethyl]-7-[[4-(4-morpholinyl)phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

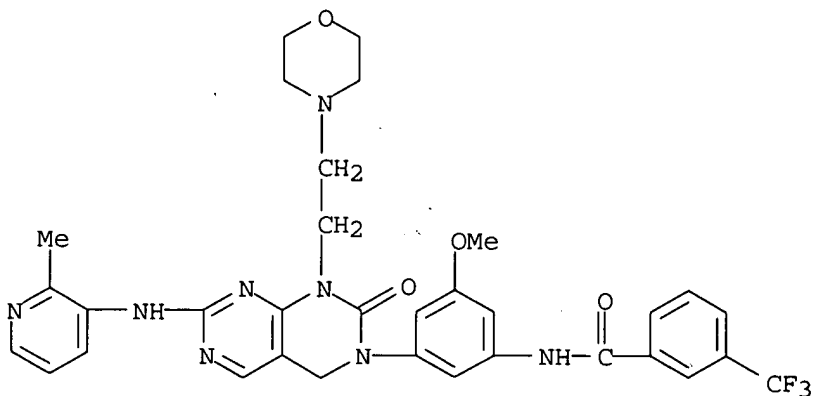
RN 839706-57-9 HCAPLUS

CN Benzamide, N-[3-[7-(cyclopropylamino)-1,4-dihydro-2-oxo-1-[2-(2-pyridinyl)ethyl]pyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



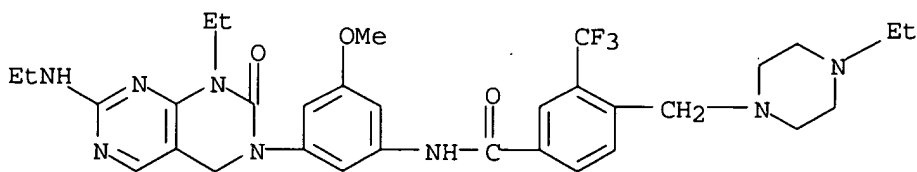
RN 839706-58-0 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-7-[(2-methyl-3-pyridinyl)amino]-1-[2-(4-morpholinyl)ethyl]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839706-59-1 HCAPLUS

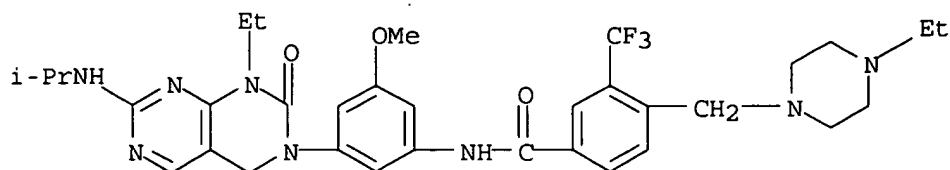
CN Benzamide, N-[3-[1-ethyl-7-(ethylamino)-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-4-[(4-ethyl-1-piperazinyl)methyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839706-60-4 HCAPLUS

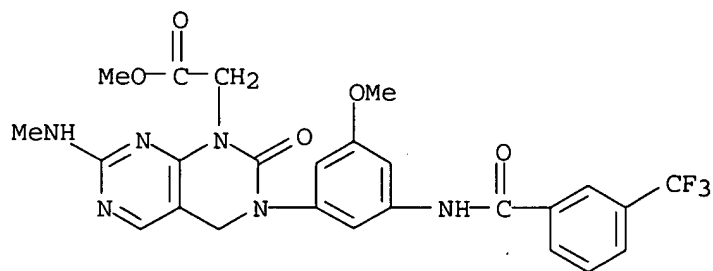
CN Benzamide, N-[3-[1-ethyl-1,4-dihydro-7-[(1-methylethyl)amino]-2-

oxypyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-4-[(4-ethyl-1-piperazinyl)methyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



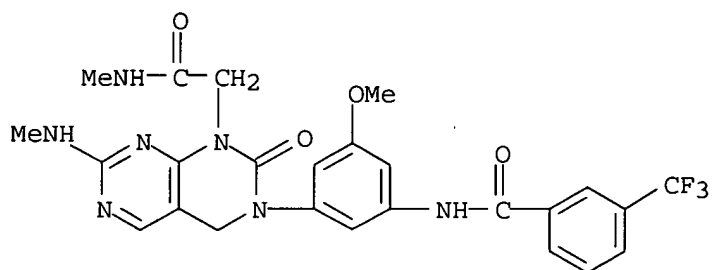
RN 839706-61-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetic acid, 3,4-dihydro-3-[3-methoxy-5-[[3-(trifluoromethyl)benzoyl]amino]phenyl]-7-(methylamino)-2-oxo-, methyl ester (9CI) (CA INDEX NAME)



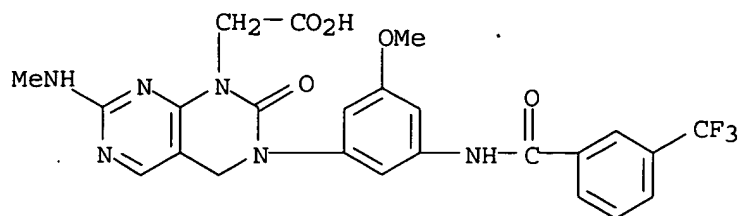
RN 839706-62-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetamide, 3,4-dihydro-3-[3-methoxy-5-[[3-(trifluoromethyl)benzoyl]amino]phenyl]-N-methyl-7-(methylamino)-2-oxo- (9CI) (CA INDEX NAME)



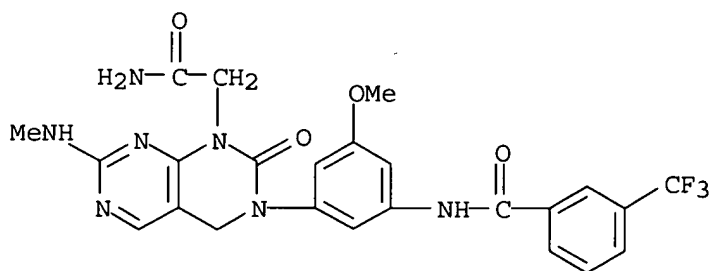
RN 839706-63-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetic acid, 3,4-dihydro-3-[3-methoxy-5-[[3-(trifluoromethyl)benzoyl]amino]phenyl]-7-(methylamino)-2-oxo- (9CI) (CA INDEX NAME)



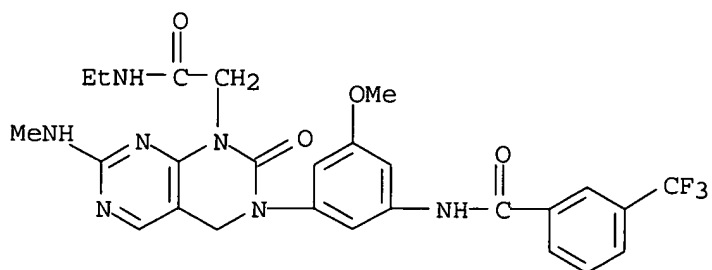
RN 839706-64-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetamide, 3,4-dihydro-3-[3-methoxy-5-[[3-(trifluoromethyl)benzoyl]amino]phenyl]-7-(methylamino)-2-oxo- (9CI) (CA INDEX NAME)



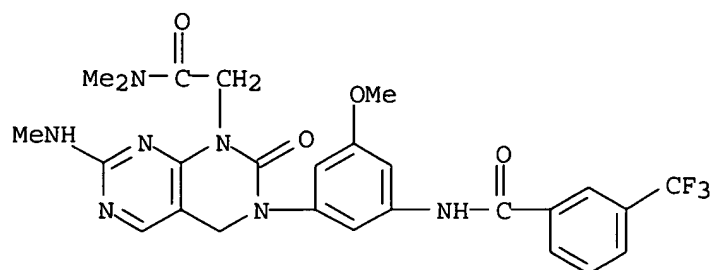
RN 839706-65-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetamide, N-ethyl-3,4-dihydro-3-[3-methoxy-5-[[3-(trifluoromethyl)benzoyl]amino]phenyl]-7-(methylamino)-2-oxo- (9CI) (CA INDEX NAME)



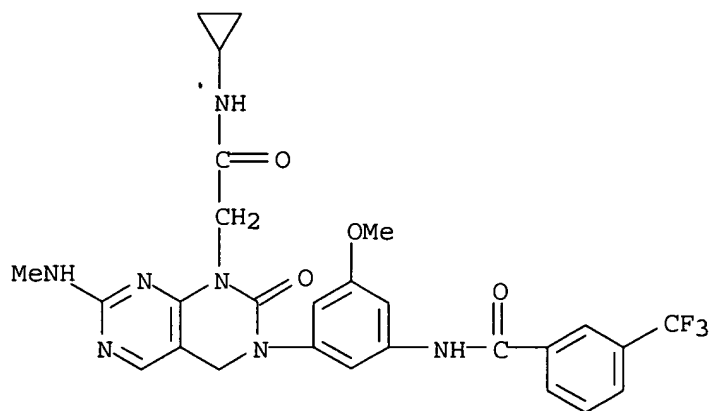
RN 839706-66-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetamide, 3,4-dihydro-3-[3-methoxy-5-[[3-(trifluoromethyl)benzoyl]amino]phenyl]-N,N-dimethyl-7-(methylamino)-2-oxo- (9CI) (CA INDEX NAME)



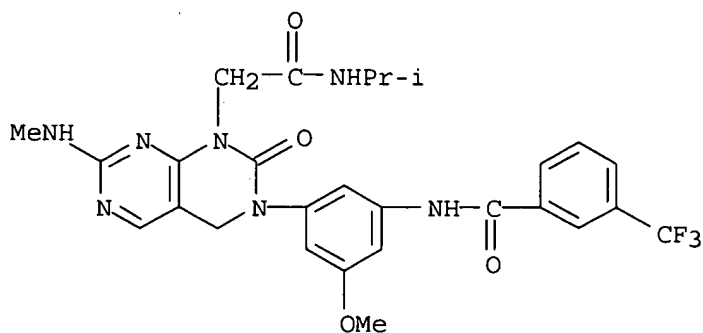
RN 839706-67-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetamide, N-cyclopropyl-3,4-dihydro-3-[3-methoxy-5-[[3-(trifluoromethyl)benzoyl]amino]phenyl]-7-(methylamino)-2-oxo- (9CI) (CA INDEX NAME)



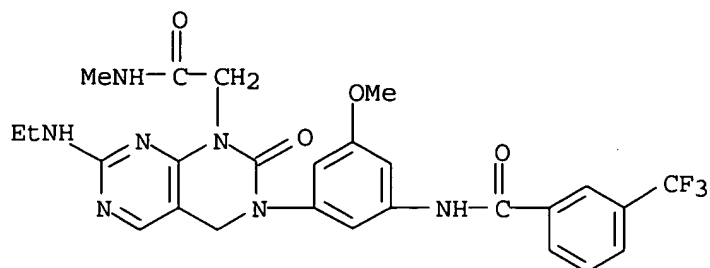
RN 839706-68-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetamide, 3,4-dihydro-3-[3-methoxy-5-[[3-(trifluoromethyl)benzoyl]amino]phenyl]-7-(methylamino)-N-(1-methylethyl)-2-oxo- (9CI) (CA INDEX NAME)



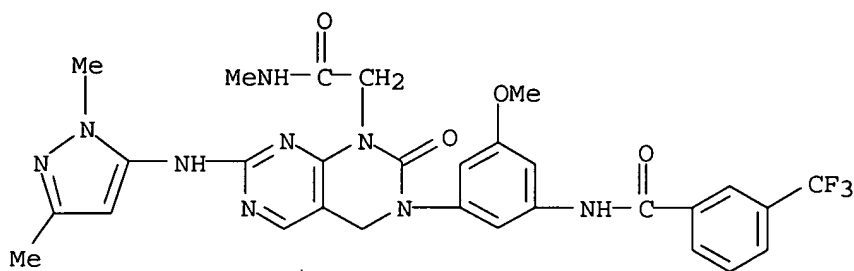
RN 839706-69-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetamide, 7-(ethylamino)-3,4-dihydro-3-[3-methoxy-5-[[3-(trifluoromethyl)benzoyl]amino]phenyl]-N-methyl-2-oxo- (9CI) (CA INDEX NAME)



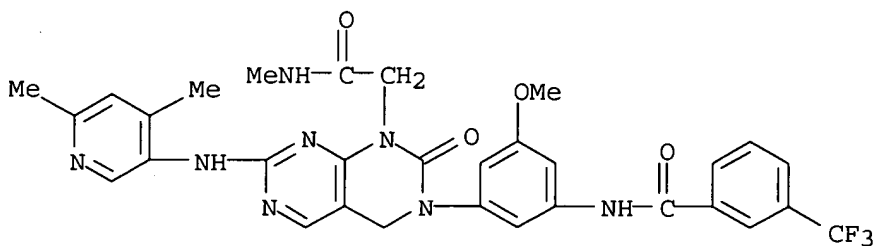
RN 839706-70-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetamide, 7-[(1,3-dimethyl-1H-pyrazol-5-yl)amino]-3,4-dihydro-3-[3-methoxy-5-[[3-(trifluoromethyl)benzoyl]amino]phenyl]-N-methyl-2-oxo- (9CI) (CA INDEX NAME)



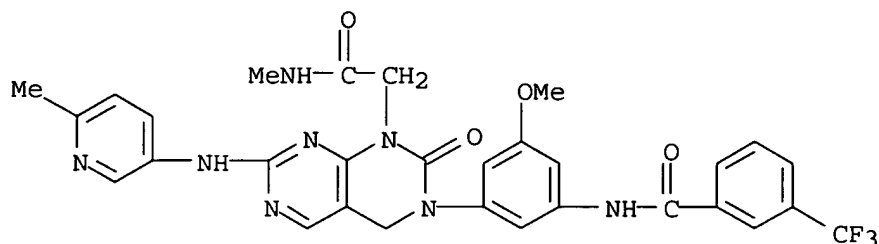
RN 839706-71-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetamide, 7-[(4,6-dimethyl-3-pyridinyl)amino]-3,4-dihydro-3-[3-methoxy-5-[[3-(trifluoromethyl)benzoyl]amino]phenyl]-N-methyl-2-oxo- (9CI) (CA INDEX NAME)



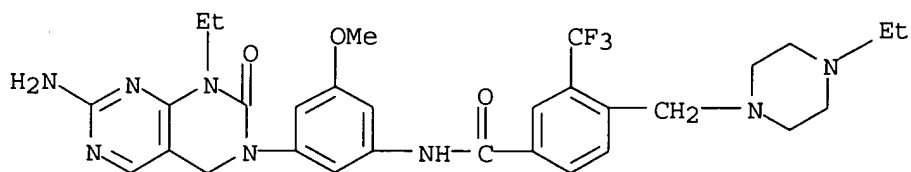
RN 839706-72-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetamide, 3,4-dihydro-3-[3-methoxy-5-[[3-(trifluoromethyl)benzoyl]amino]phenyl]-N-methyl-7-[(6-methyl-3-pyridinyl)amino]-2-oxo- (9CI) (CA INDEX NAME)



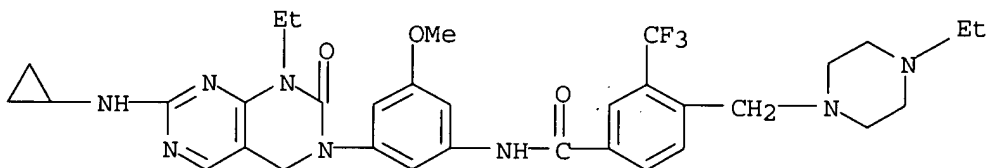
RN 839706-73-9 HCAPLUS

CN Benzamide, N-[3-(7-amino-1-ethyl-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl)-5-methoxyphenyl]-4-[(4-ethyl-1-piperazinyl)methyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839706-74-0 HCAPLUS

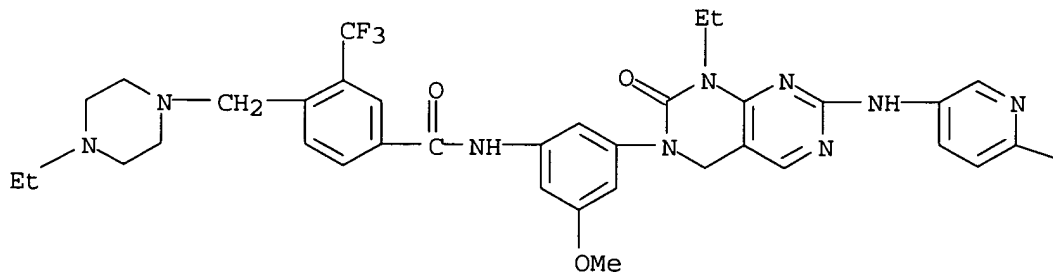
CN Benzamide, N-[3-[7-(cyclopropylamino)-1-ethyl-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-4-[(4-ethyl-1-piperazinyl)methyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839706-75-1 HCAPLUS

CN Benzamide, N-[3-[1-ethyl-1,4-dihydro-7-[(6-methyl-3-pyridinyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-4-[(4-ethyl-1-piperazinyl)methyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

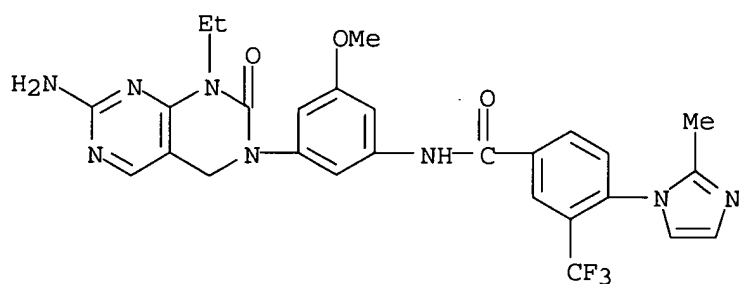


PAGE 1-B

Me

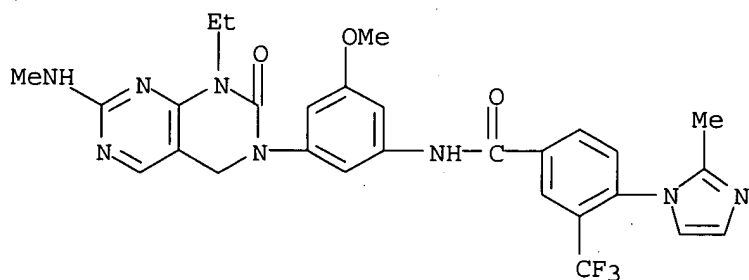
RN 839706-76-2 HCAPLUS

CN Benzamide, N-[3-(7-amino-1-ethyl-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl)-5-methoxyphenyl]-4-(2-methyl-1H-imidazol-1-yl)-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



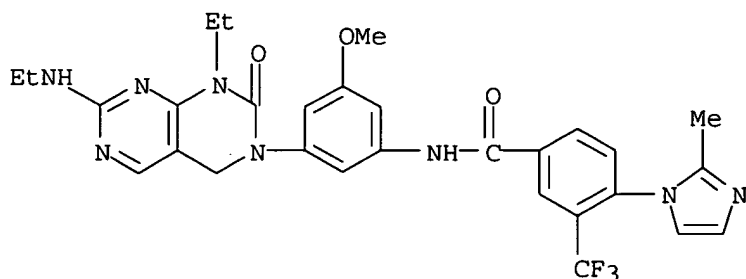
RN 839706-77-3 HCAPLUS

CN Benzamide, N-[3-[1-ethyl-1,4-dihydro-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-4-(2-methyl-1H-imidazol-1-yl)-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



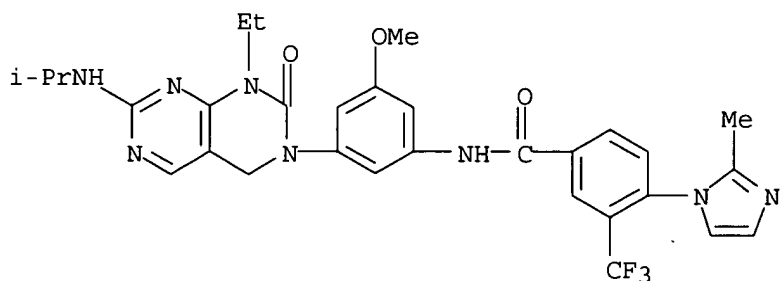
RN 839706-78-4 HCAPLUS

CN Benzamide, N-[3-[1-ethyl-7-(ethylamino)-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-4-(2-methyl-1H-imidazol-1-yl)-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



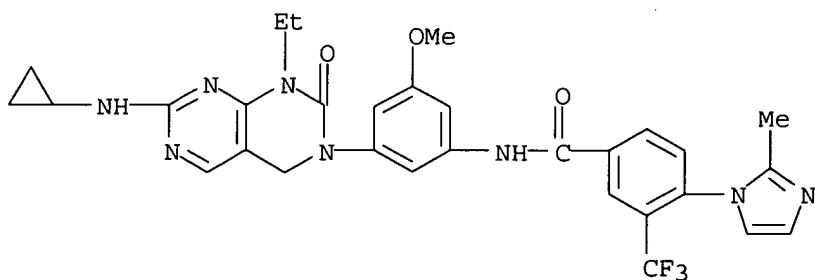
RN 839706-79-5 HCAPLUS

CN Benzamide, N-[3-[1-ethyl-1,4-dihydro-7-[(1-methylethyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-4-(2-methyl-1H-imidazol-1-yl)-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



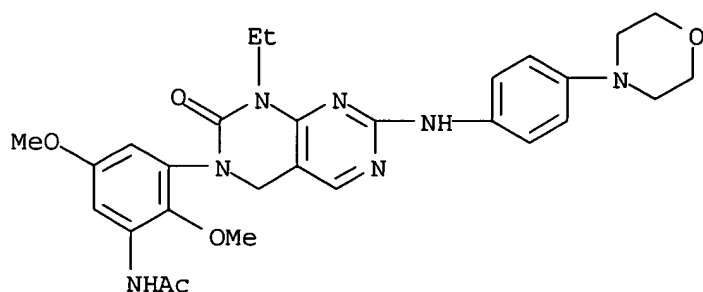
RN 839706-80-8 HCAPLUS

CN Benzamide, N-[3-[7-(cyclopropylamino)-1-ethyl-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-4-(2-methyl-1H-imidazol-1-yl)-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



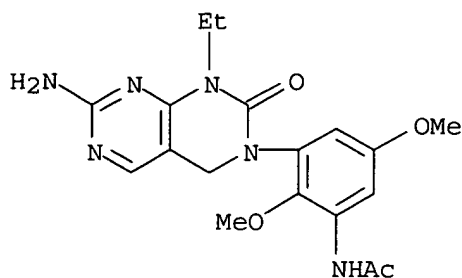
RN 839706-81-9 HCAPLUS

CN Acetamide, N-[3-[1-ethyl-1,4-dihydro-7-[[4-(4-morpholinyl)phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-2,5-dimethoxyphenyl]- (9CI) (CA INDEX NAME)



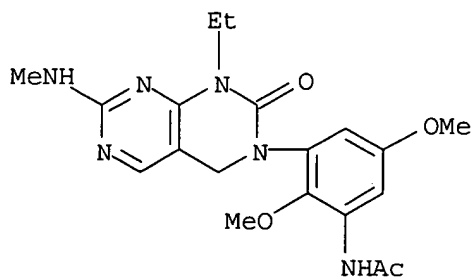
RN 839706-82-0 HCAPLUS

CN Acetamide, N-[3-(7-amino-1-ethyl-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl)-2,5-dimethoxyphenyl]- (9CI) (CA INDEX NAME)



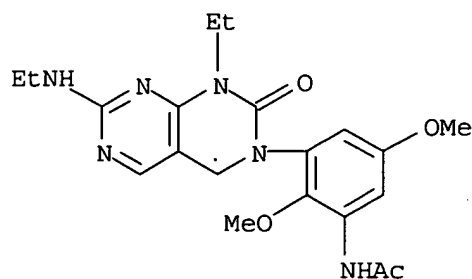
RN 839706-83-1 HCAPLUS

CN Acetamide, N-[3-[1-ethyl-1,4-dihydro-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-2,5-dimethoxyphenyl]- (9CI) (CA INDEX NAME)



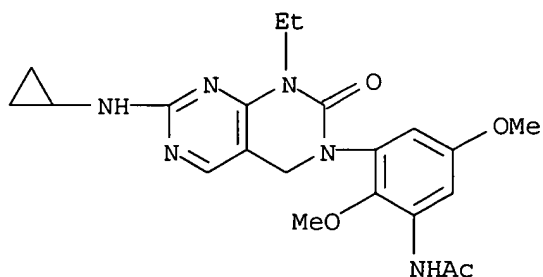
RN 839706-84-2 HCAPLUS

CN Acetamide, N-[3-[1-ethyl-7-(ethylamino)-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-2,5-dimethoxyphenyl]- (9CI) (CA INDEX NAME)



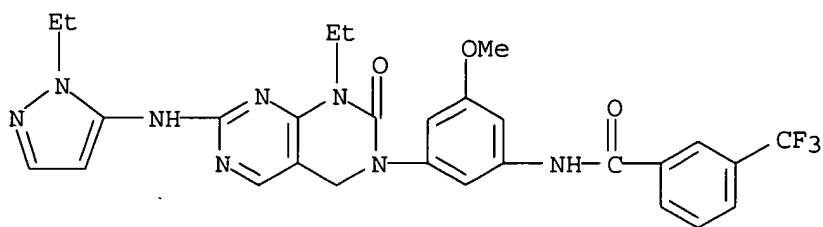
RN 839706-85-3 HCAPLUS

CN Acetamide, N-[3-[7-(cyclopropylamino)-1-ethyl-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-2,5-dimethoxyphenyl]-(9CI) (CA INDEX NAME)



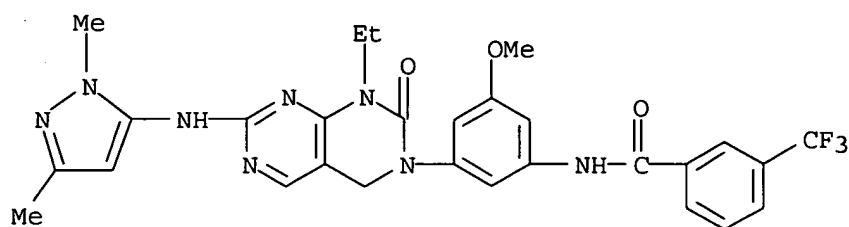
RN 839706-86-4 HCAPLUS

CN Benzamide, N-[3-[1-ethyl-7-[(1-ethyl-1H-pyrazol-5-yl)amino]-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



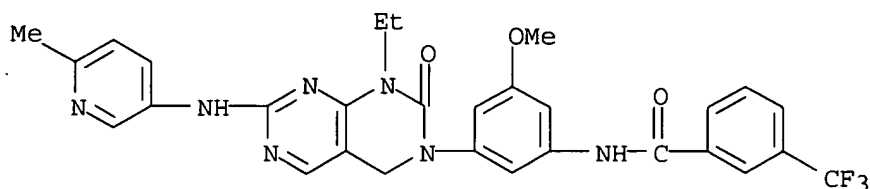
RN 839706-87-5 HCAPLUS

CN Benzamide, N-[3-[7-[(1,3-dimethyl-1H-pyrazol-5-yl)amino]-1-ethyl-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



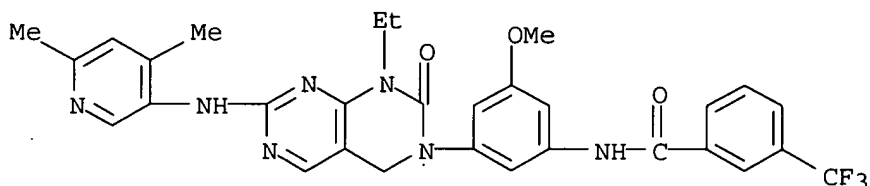
RN 839706-88-6 HCAPLUS

CN Benzamide, N-[3-[1-ethyl-1,4-dihydro-7-[(6-methyl-3-pyridinyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



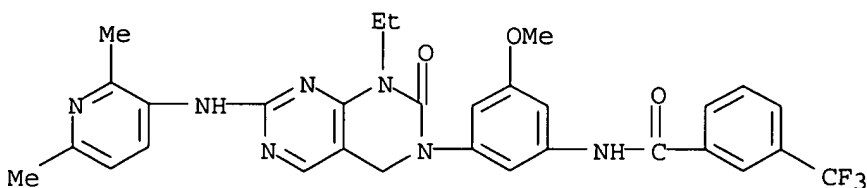
RN 839706-89-7 HCAPLUS

CN Benzamide, N-[3-[7-[(4,6-dimethyl-3-pyridinyl)amino]-1-ethyl-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



RN 839706-90-0 HCAPLUS

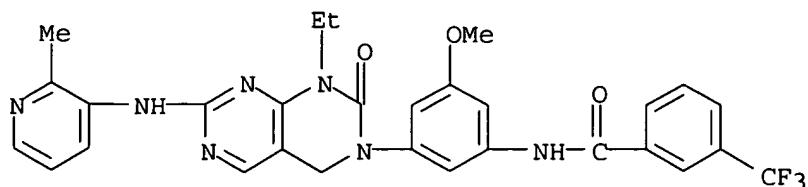
CN Benzamide, N-[3-[7-[(2,6-dimethyl-3-pyridinyl)amino]-1-ethyl-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



RN 839706-91-1 HCAPLUS

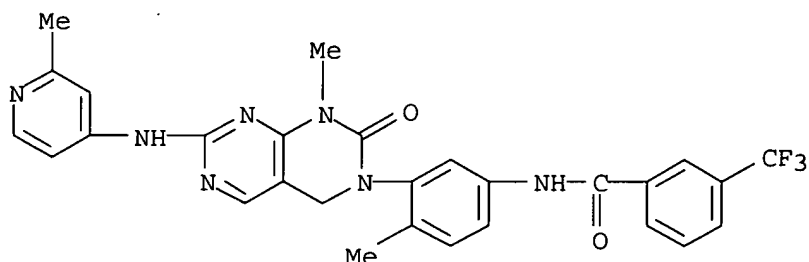
CN Benzamide, N-[3-[1-ethyl-1,4-dihydro-7-[(2-methyl-3-pyridinyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)

(9CI) (CA INDEX NAME)



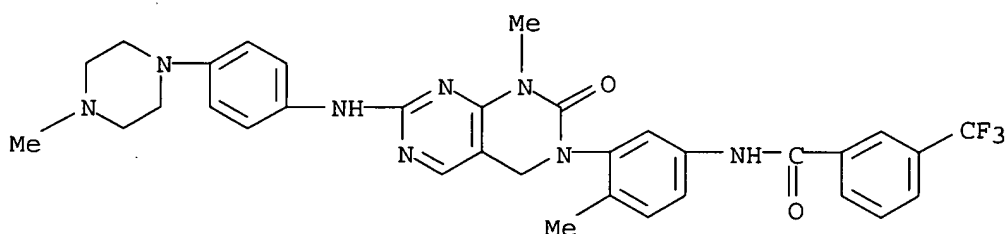
RN 839706-93-3 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[(2-methyl-4-pyridinyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839706-94-4 HCAPLUS

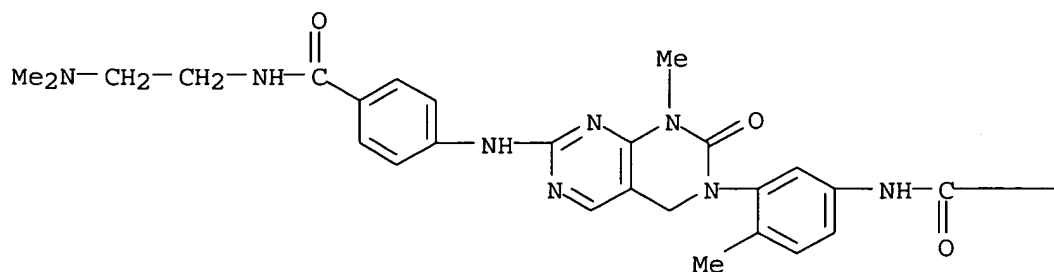
CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



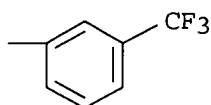
RN 839706-96-6 HCAPLUS

CN Benzamide, N-[3-[7-[[4-[[2-(dimethylamino)ethyl]amino]carbonyl]phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

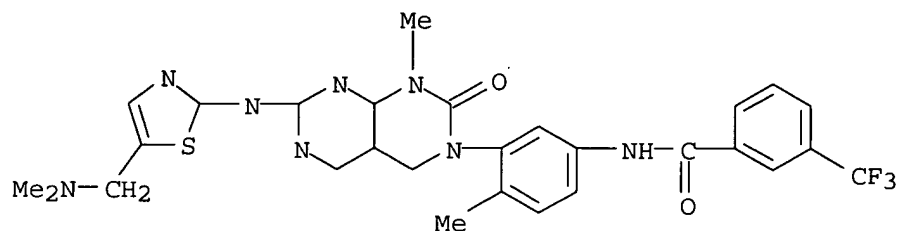


PAGE 1-B



RN 839706-97-7 HCAPLUS

CN Benzamide, N-[3-[7-[[5-[(dimethylamino)methyl]-2-thiazolyl]amino]-1,4-dihydro-1-methyl-2-oxypyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

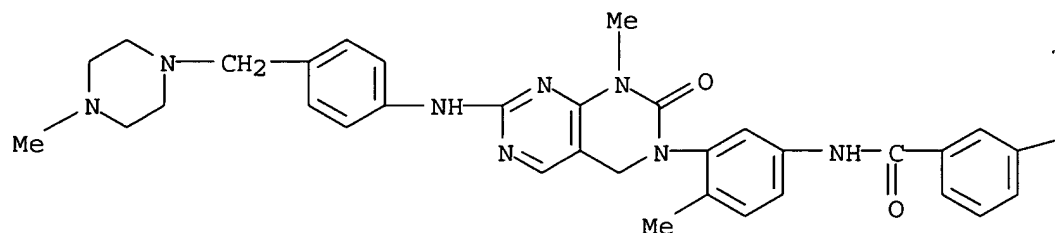


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 839706-98-8 HCAPLUS

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PAGE 1-A

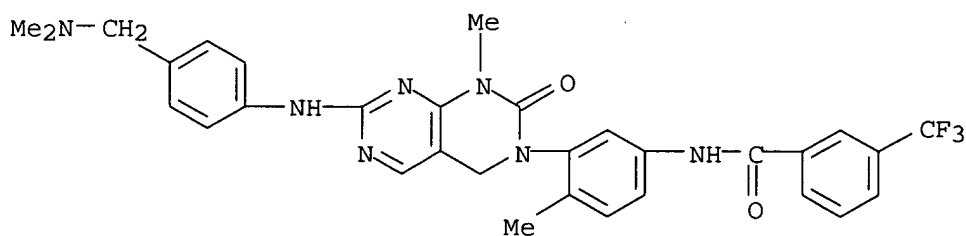


PAGE 1-B

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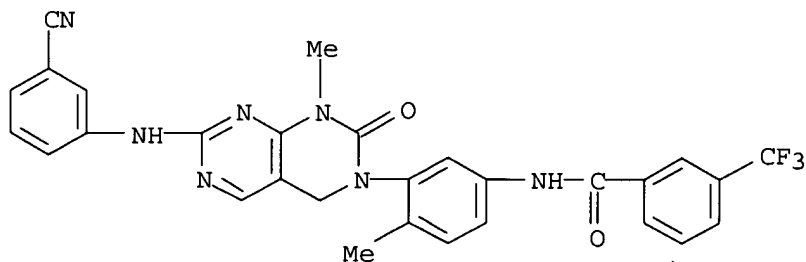
RN 839706-99-9 HCAPLUS

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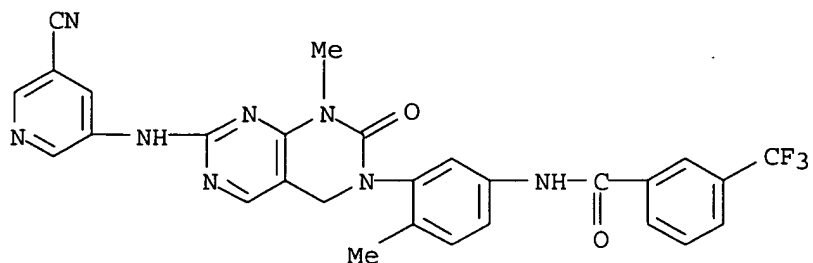
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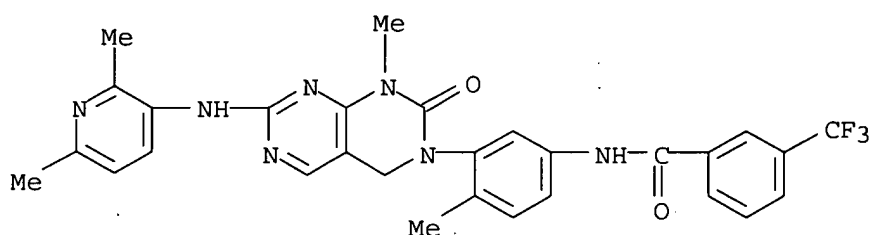
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CN Benzamide, N-[3-[7-[(5-cyano-3-pyridinyl)amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



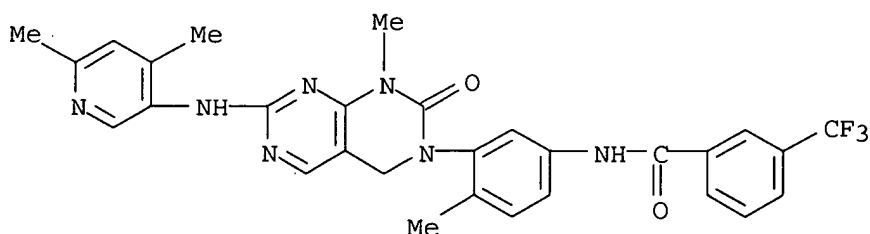
RN 839707-02-7 HCAPLUS

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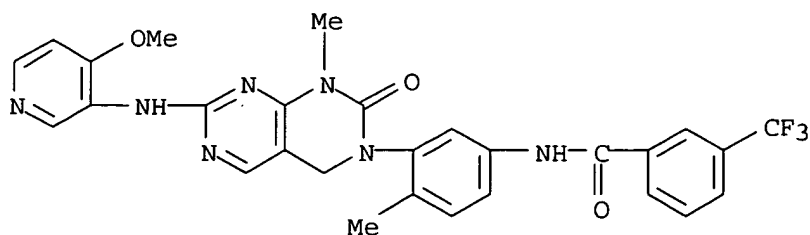
RN 839707-03-8 HCAPLUS

CN Benzamide, N-[3-[7-[(4,6-dimethyl-3-pyridinyl)amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



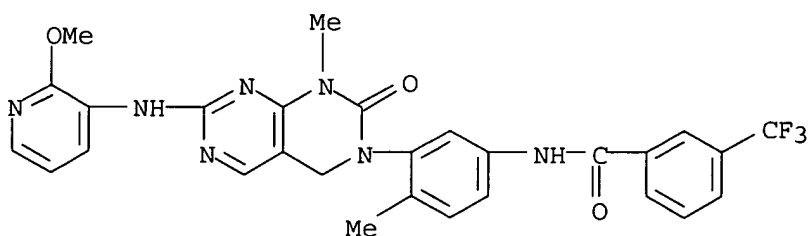
RN 839707-04-9 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-7-[(4-methoxy-3-pyridinyl)amino]-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



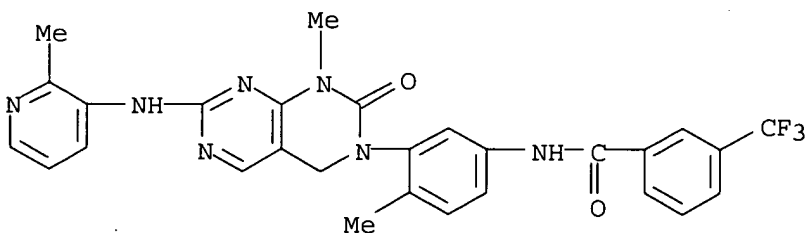
RN 839707-05-0 HCAPLUS

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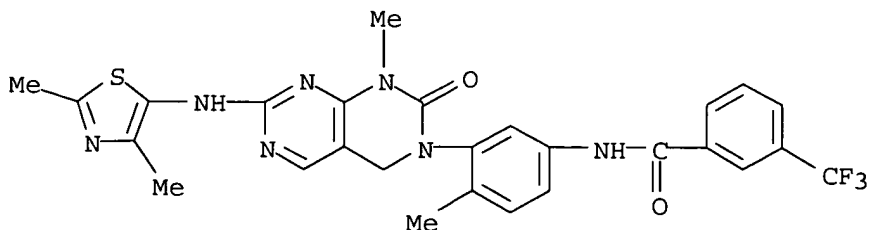
RN 839707-06-1 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[(2-methyl-3-pyridinyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



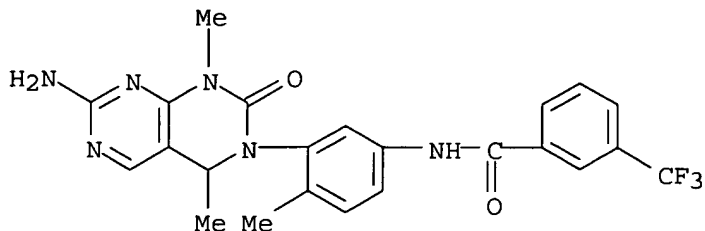
RN 839707-07-2 HCAPLUS

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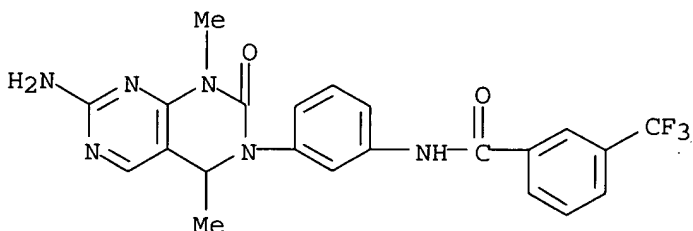
RN 839707-08-3 HCAPLUS

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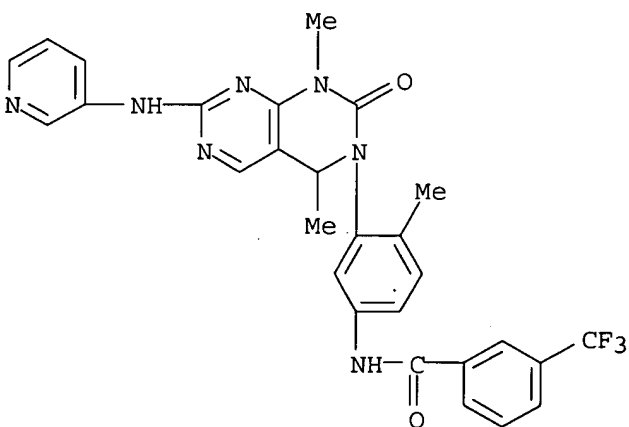
RN 839707-09-4 HCAPLUS

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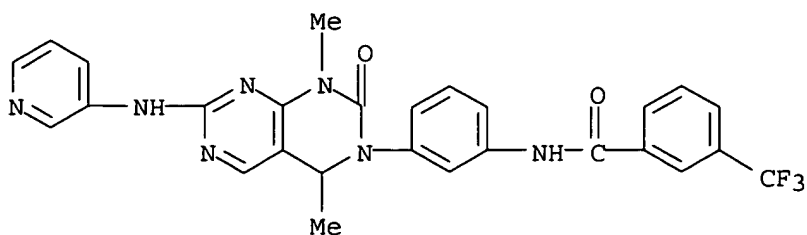
RN 839707-10-7 HCAPLUS

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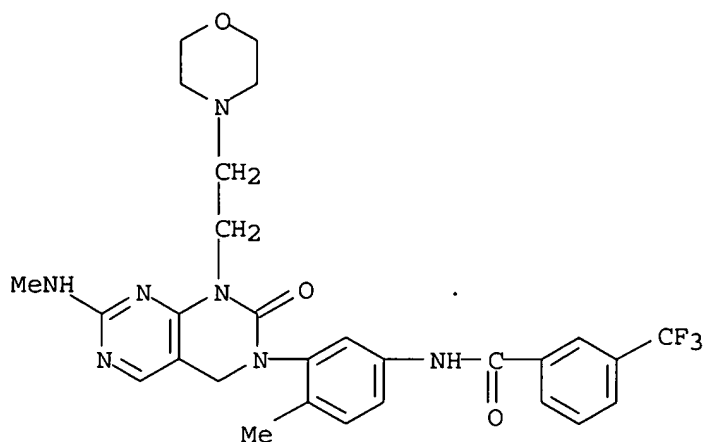
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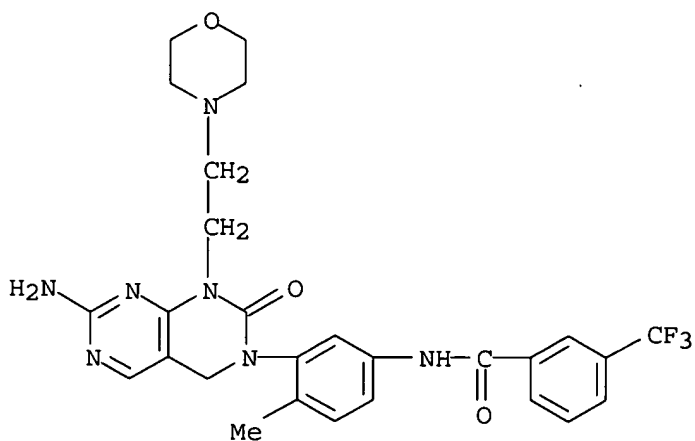
RN 839707-12-9 HCAPLUS

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RN 839707-13-0 HCAPLUS

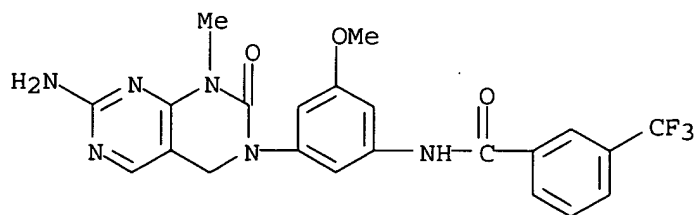
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RN 839707-14-1 HCAPLUS

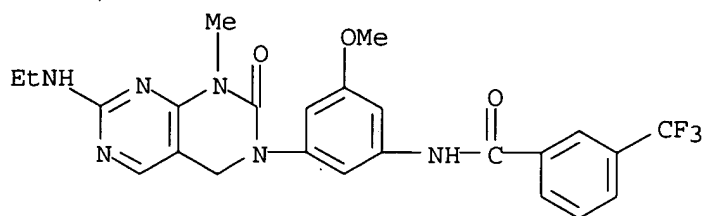
CN Benzamide, N-[3-(7-amino-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-

d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



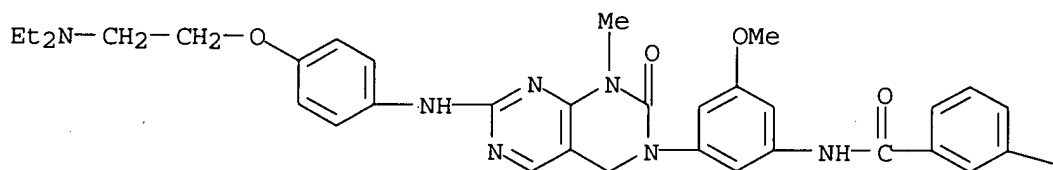
RN 839707-15-2 HCAPLUS

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RN 839707-16-3 HCAPLUS

CN Benzamide, N-[3-[7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



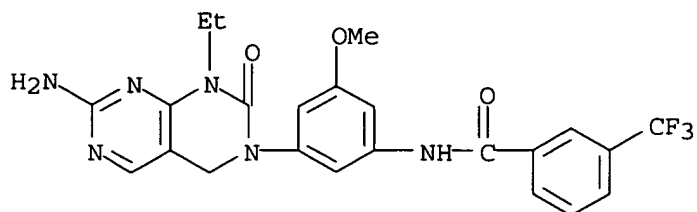
PAGE 1-A

PAGE 1-B

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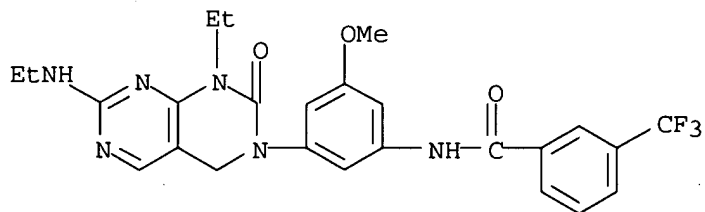
RN 839707-17-4 HCAPLUS

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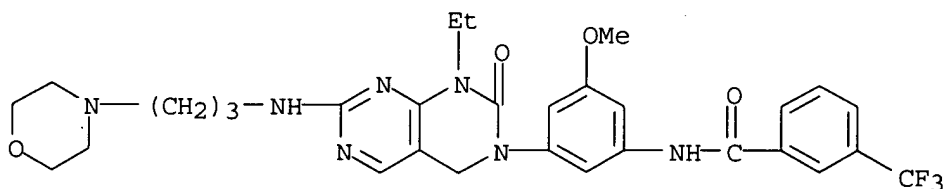
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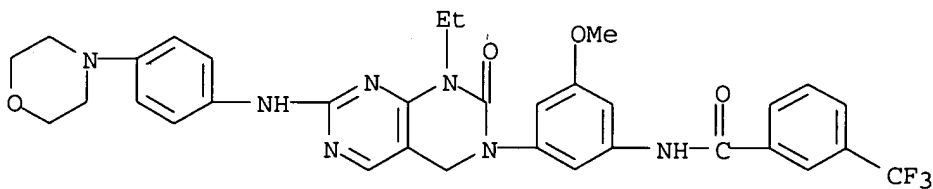
RN 839707-19-6 HCAPLUS

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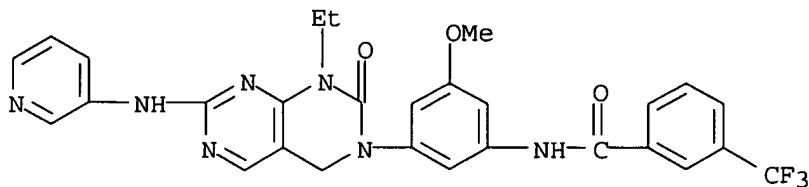
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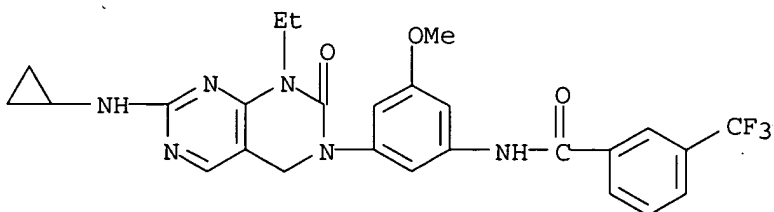
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CN Benzamide, N-[3-[1-ethyl-1,4-dihydro-2-oxo-7-(3-pyridinylamino)pyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



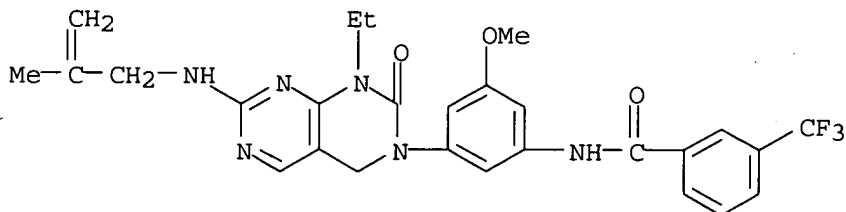
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CN Benzamide, N-[3-[7-(cyclopropylamino)-1-ethyl-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



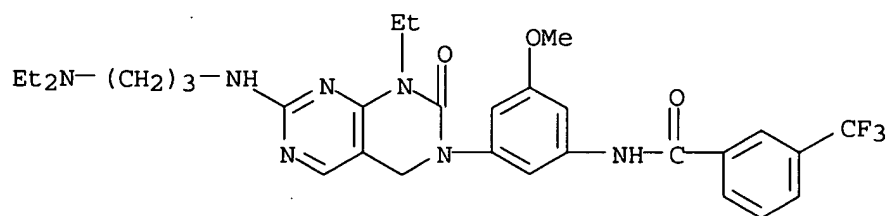
RN 839707-23-2 HCAPLUS

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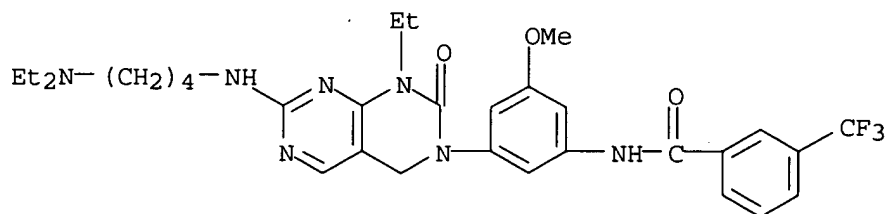
RN 839707-24-3 HCAPLUS

CN Benzamide, N-[3-[7-[[3-(diethylamino)propyl]amino]-1-ethyl-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



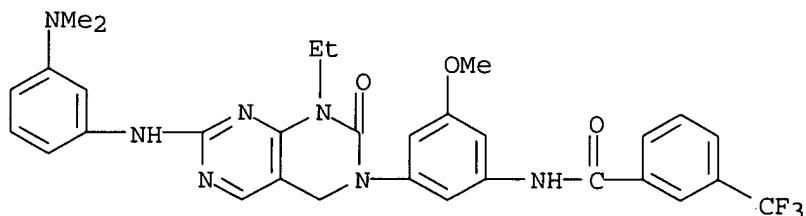
RN 839707-25-4 HCAPLUS

CN Benzamide, N-[3-[7-[[4-(diethylamino)butyl]amino]-1-ethyl-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



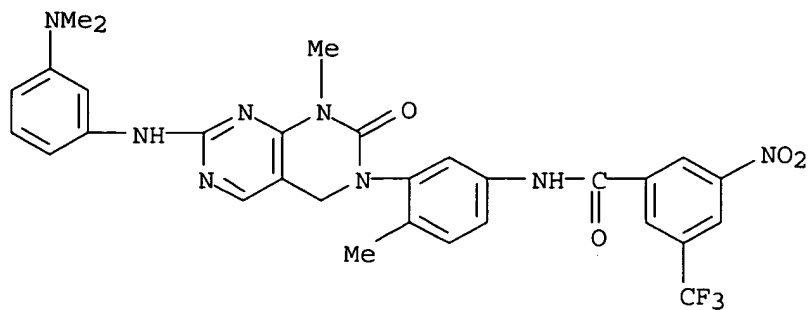
RN 839707-26-5 HCAPLUS

CN Benzamide, N-[3-[7-[[3-(dimethylamino)phenyl]amino]-1-ethyl-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-5-methoxyphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)



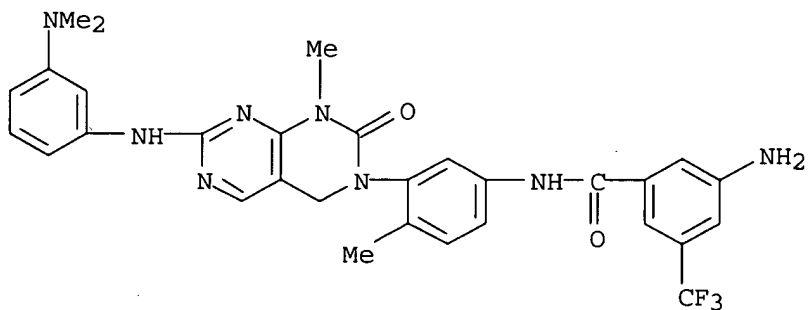
RN 839707-27-6 HCAPLUS

CN Benzamide, N-[3-[7-[[3-(dimethylamino)phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-nitro-5-(trifluoromethyl)-(9CI) (CA INDEX NAME)



RN 839707-28-7 HCAPLUS

CN Benzamide, 3-amino-N-[3-[7-[[3-(dimethylamino)phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)

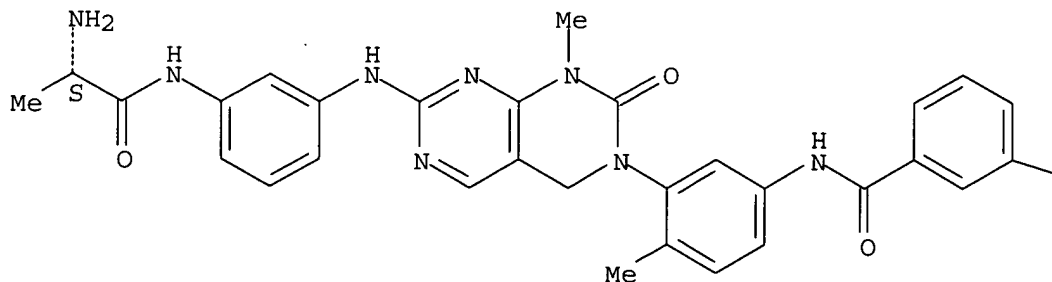


RN 839707-29-8 HCAPLUS

CN Benzamide, N-[3-[7-[[3-[[[(2S)-2-amino-1-oxopropyl]amino]phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

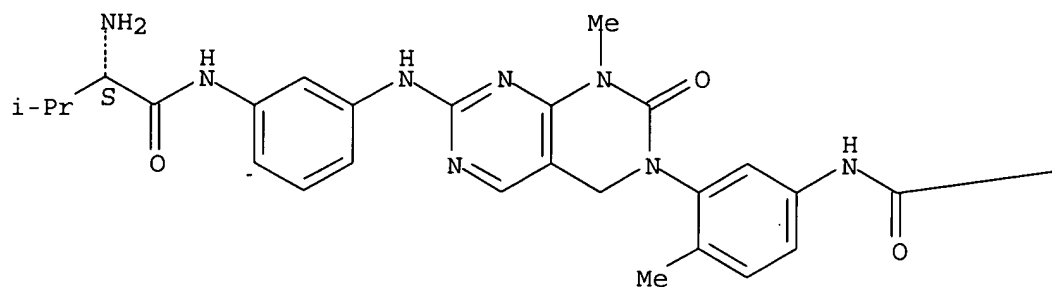
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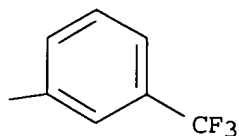
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Absolute stereochemistry.

PAGE 1-A

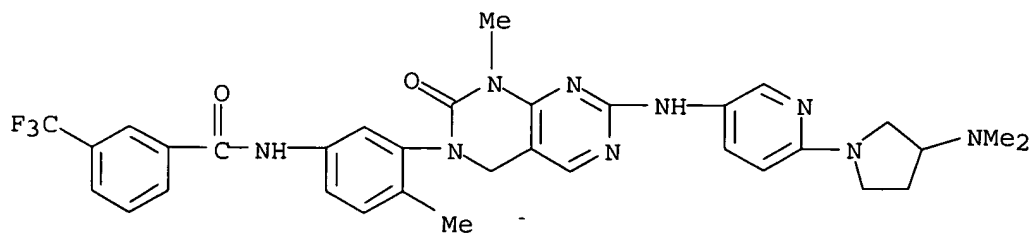


PAGE 1-B



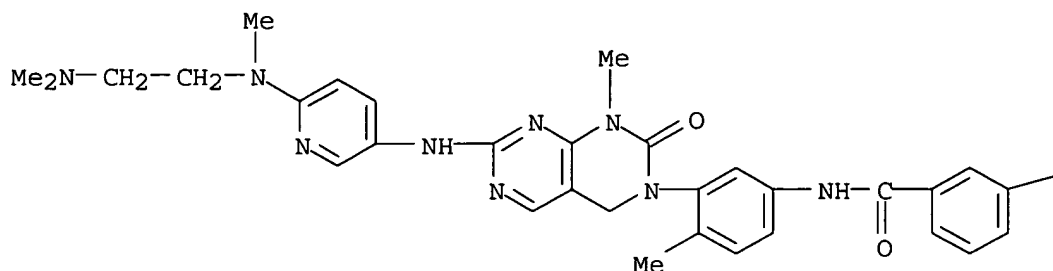
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RN 839707-32-3 HCAPLUS
 CN Benzamide, N-[3-[7-[[6-[[2-(dimethylamino)ethyl]methylamino]-3-pyridinyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

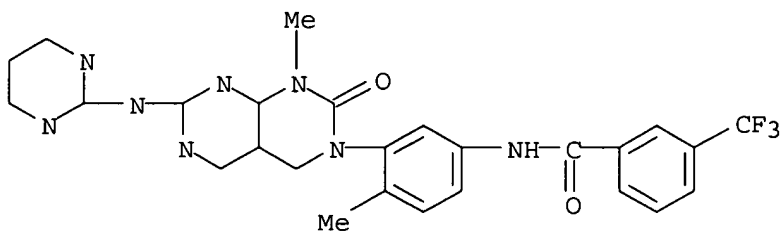
PAGE 1-A



PAGE 1-B

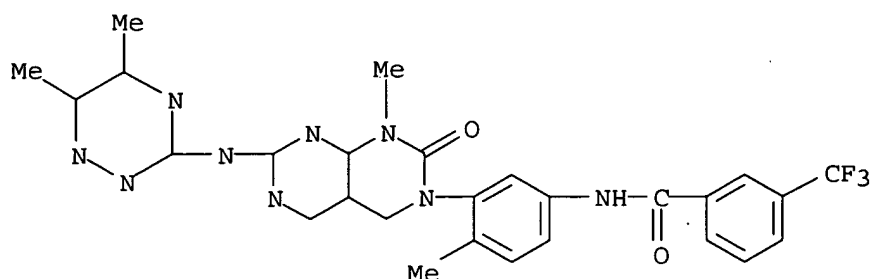
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RN 839707-33-4 HCAPLUS
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

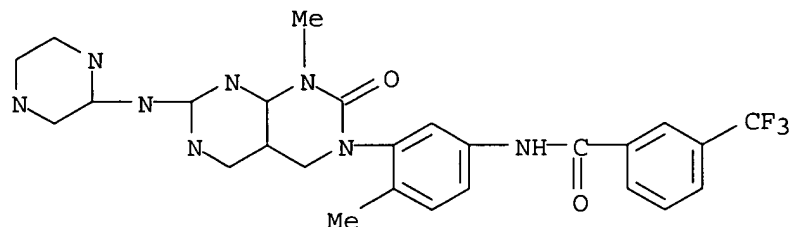
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 CN Benzamide, N-[3-[7-[(5,6-dimethyl-1,2,4-triazin-3-yl)amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 839707-35-6 HCAPLUS

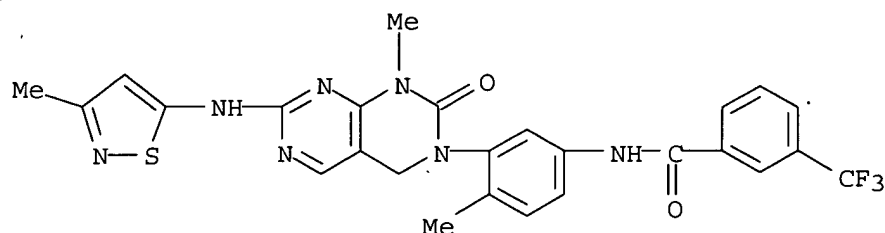
CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-(pyrazinylamino)pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

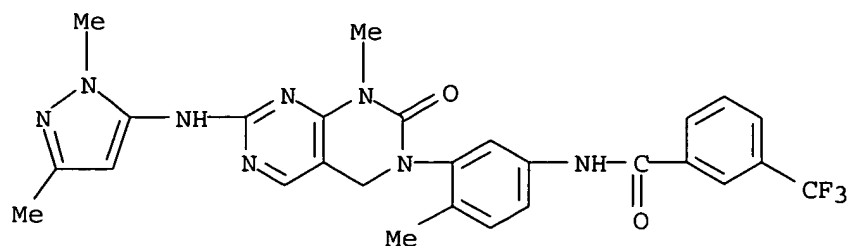
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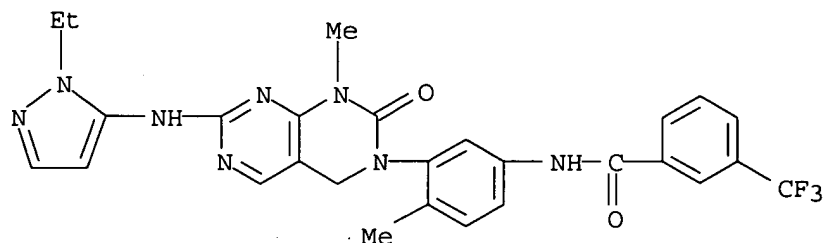
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RN 839707-38-9 HCAPLUS

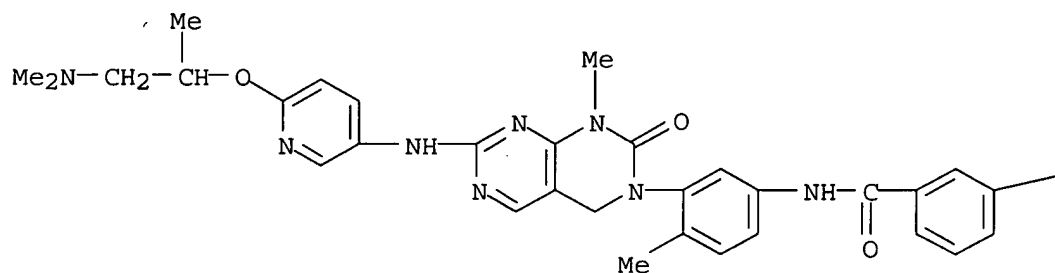
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RN 839707-39-0 HCAPLUS

CN Benzamide, N-[3-[7-[[6-[2-(dimethylamino)-1-methylethoxy]-3-pyridinyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)-(9CI) (CA INDEX NAME)

PAGE 1-A



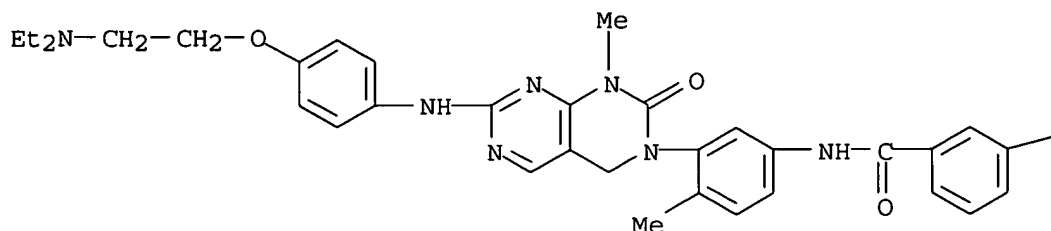
PAGE 1-B

—CF₃

RN 839707-40-3 HCAPLUS

CN Benzamide, N-[3-[7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

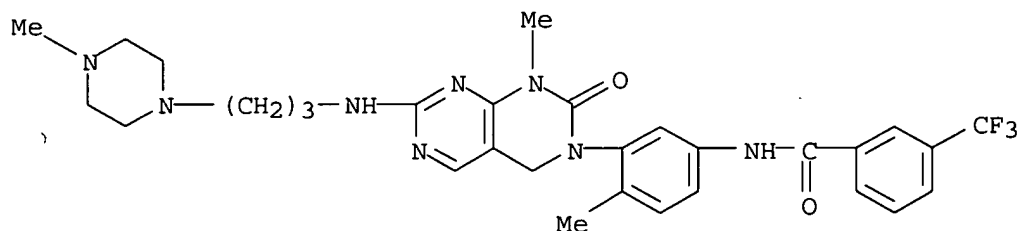


PAGE 1-B

—CF₃

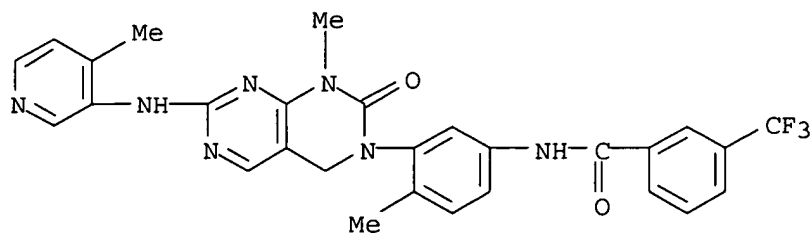
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CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[3-(4-methyl-1-piperazinyl)propyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



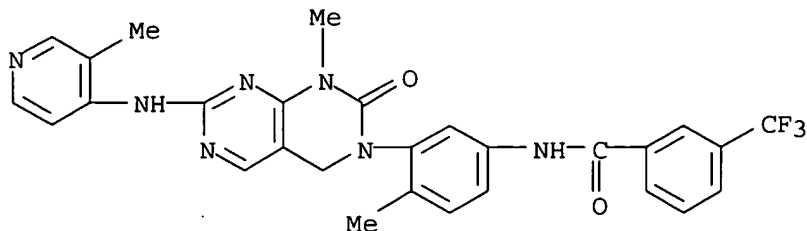
RN 839707-43-6 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[(4-methyl-3-pyridinyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



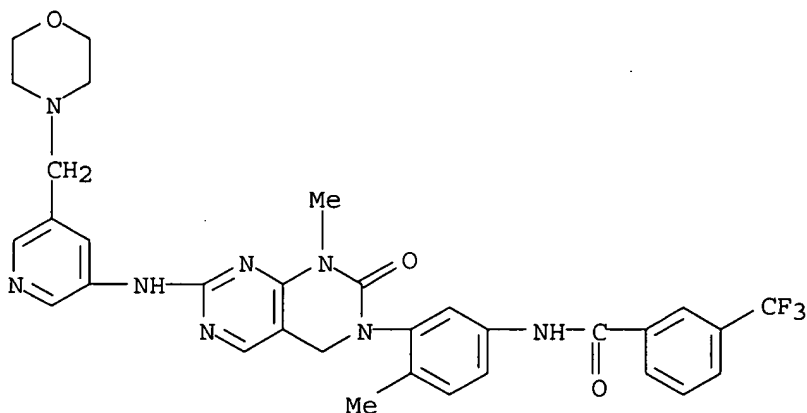
RN 839707-44-7 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[(3-methyl-4-pyridinyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



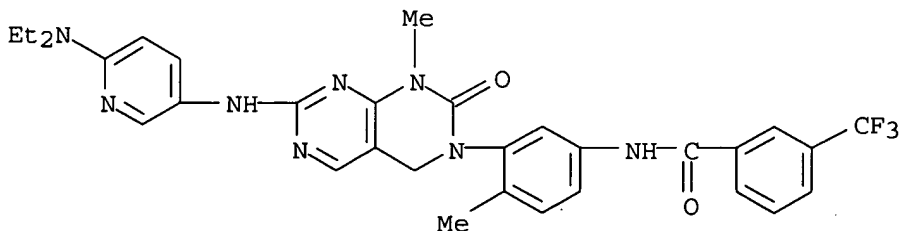
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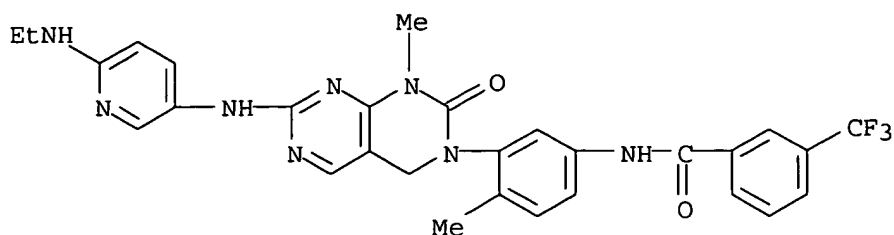
RN 839707-46-9 HCAPLUS

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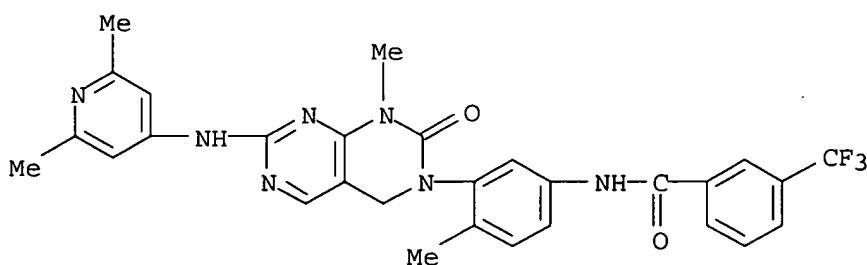
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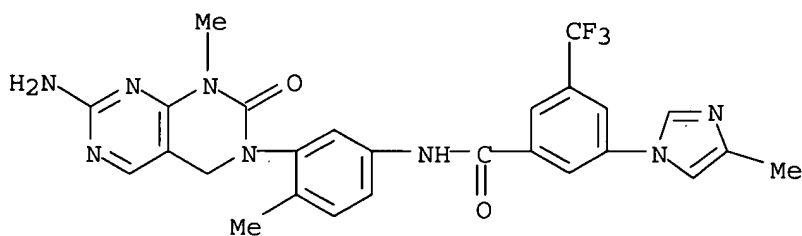
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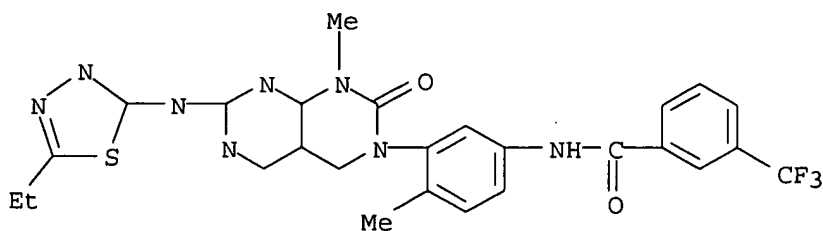
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RN 839707-50-5 HCAPLUS

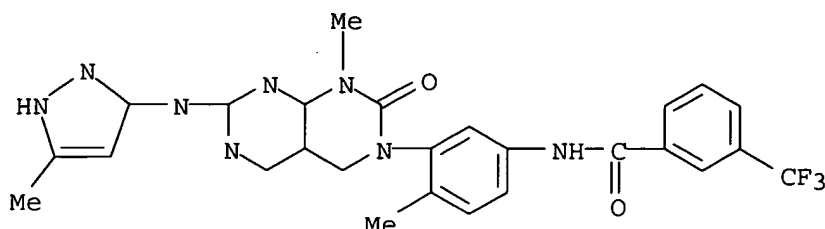
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 839707-53-8 HCAPLUS

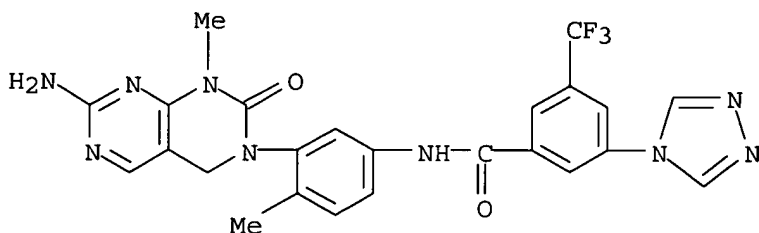
CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[(5-methyl-1H-pyrazol-3-yl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

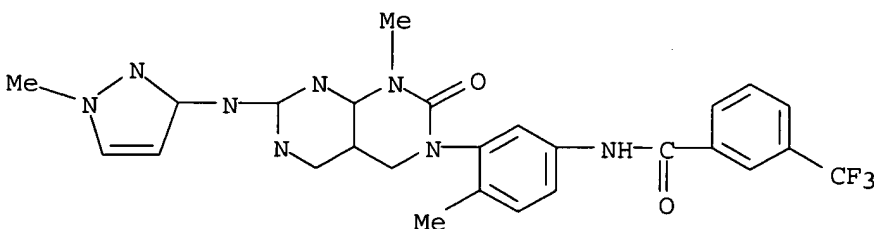
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RN 839707-55-0 HCAPLUS

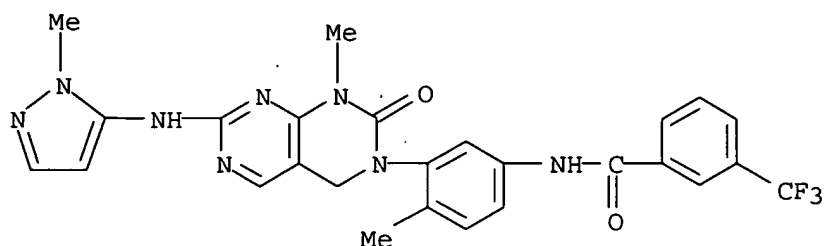
CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[(1-methyl-1H-pyrazol-3-yl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

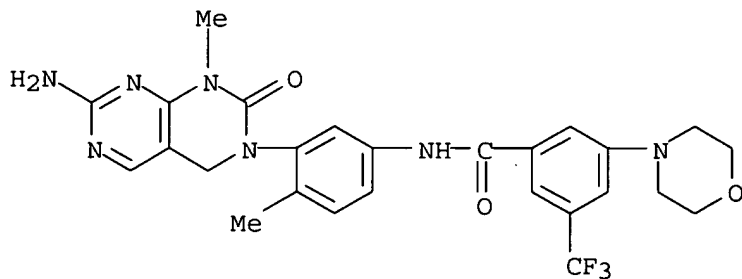
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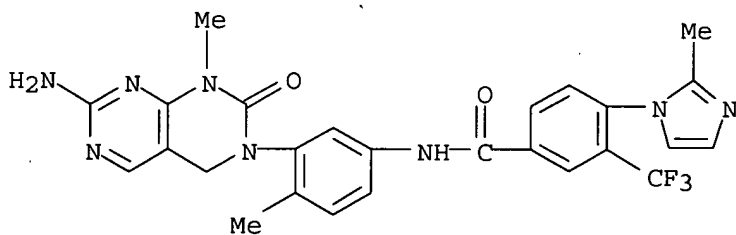
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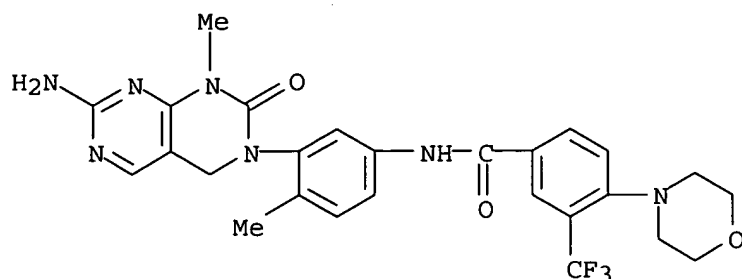
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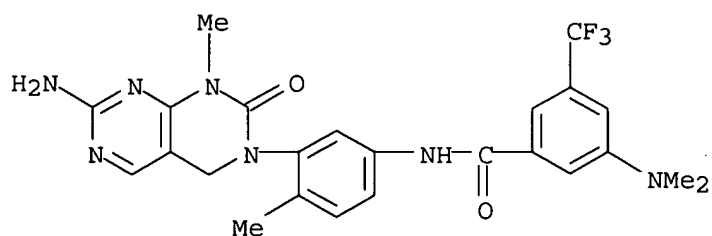
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CN Benzamide, N-[3-(7-amino-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl)-4-methylphenyl]-4-(4-morpholinyl)-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



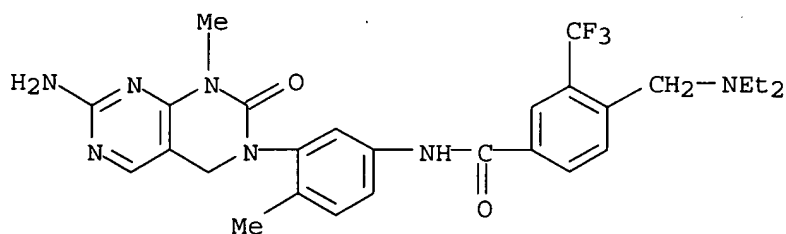
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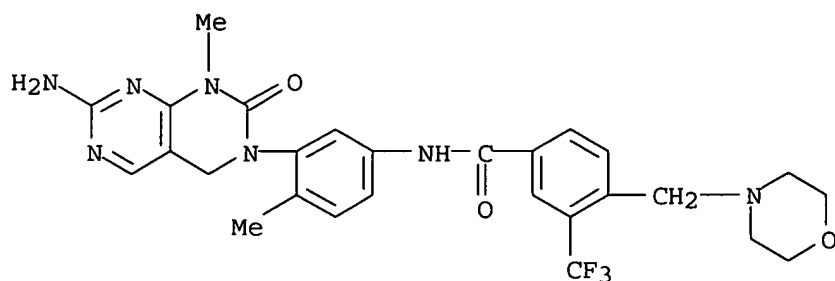
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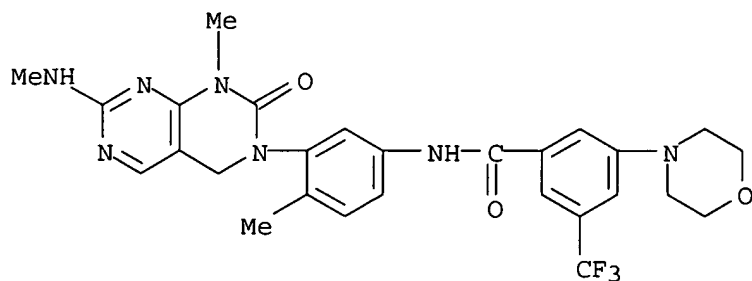
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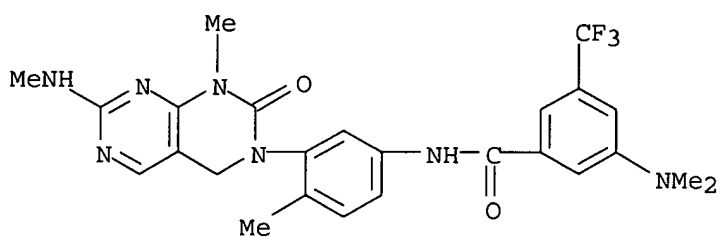
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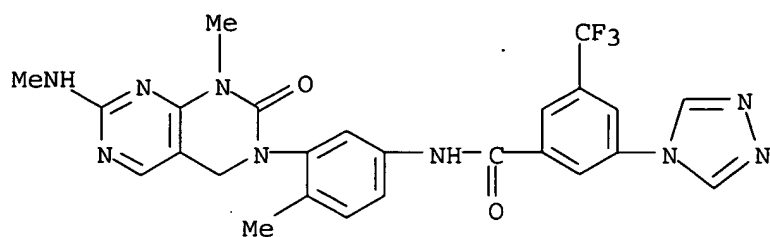
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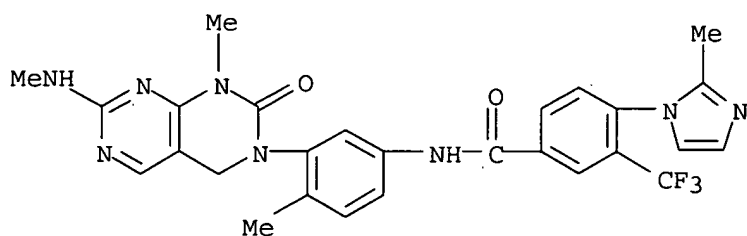
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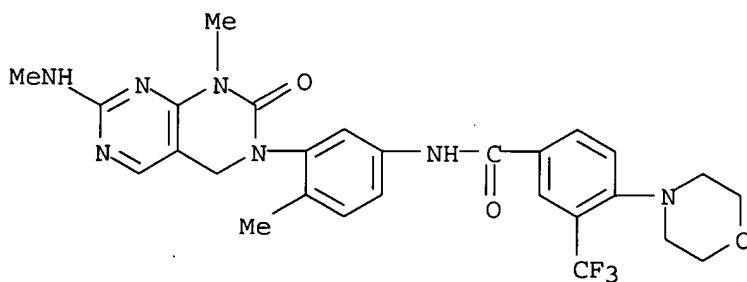
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CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-4-(2-methyl-1H-imidazol-1-yl)-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



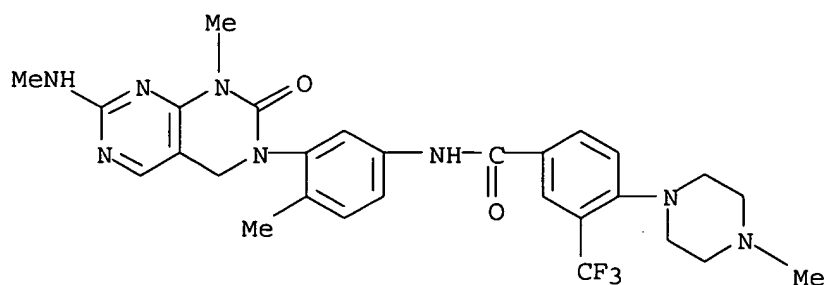
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CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-4-(4-morpholinyl)-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



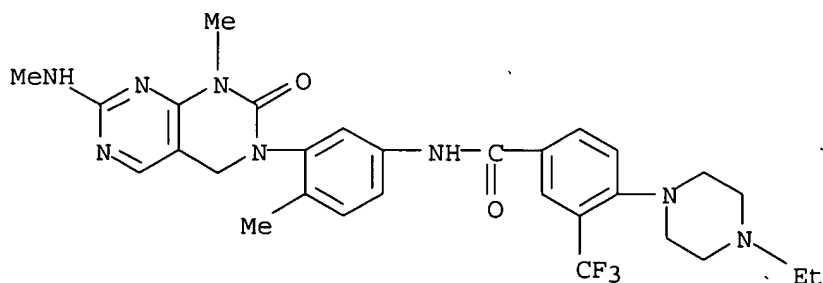
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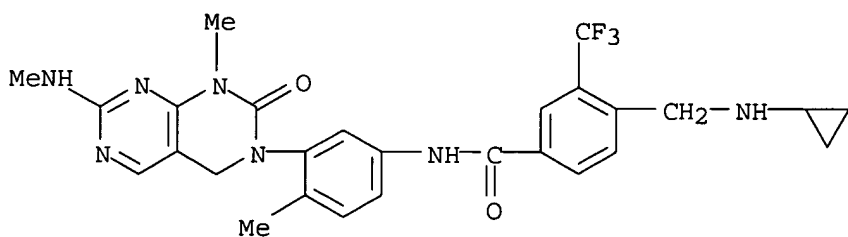
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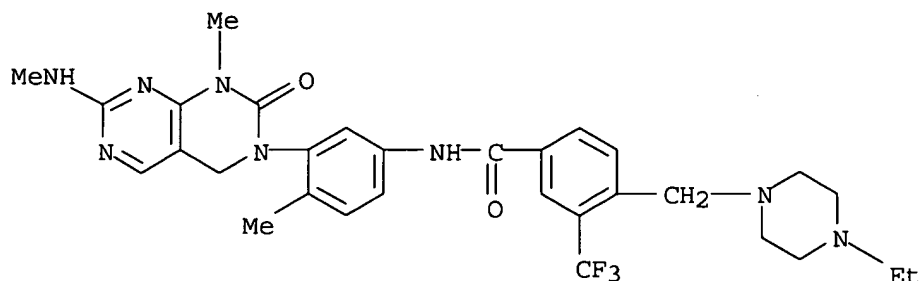
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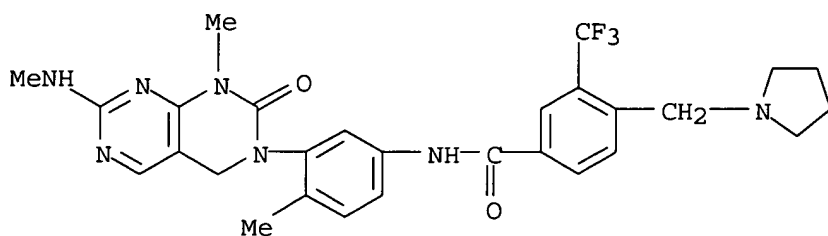
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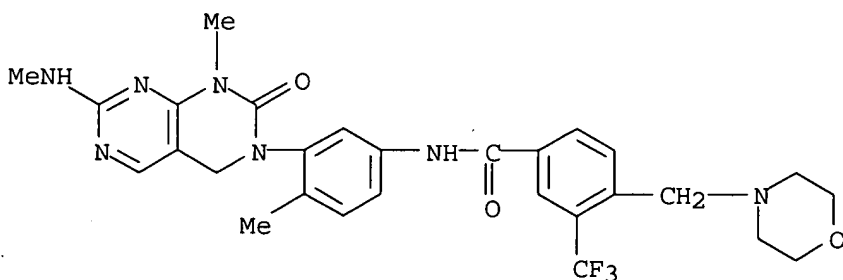
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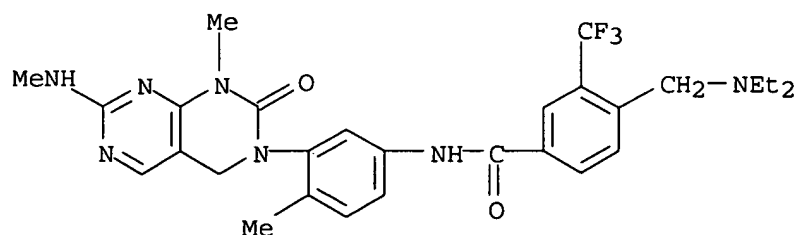
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CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-4-(4-morpholinylmethyl)-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



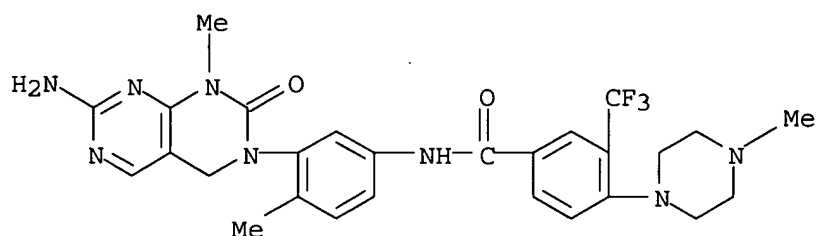
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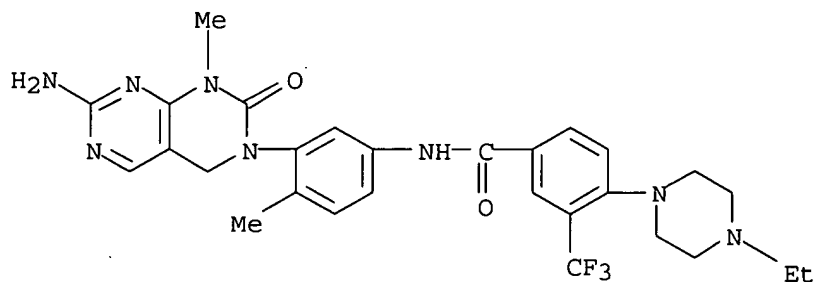
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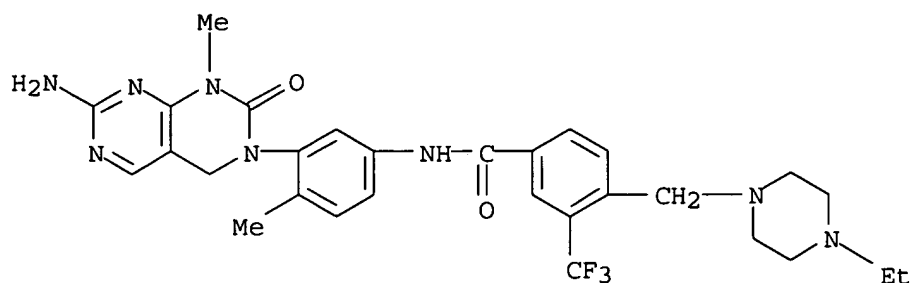
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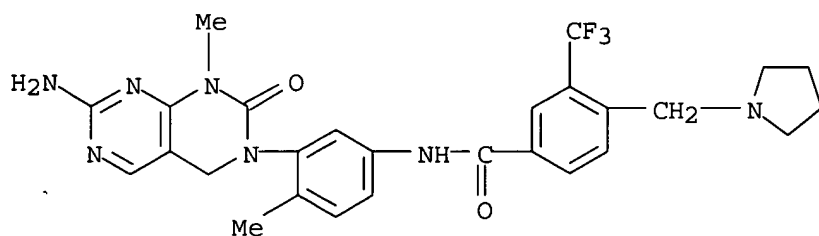
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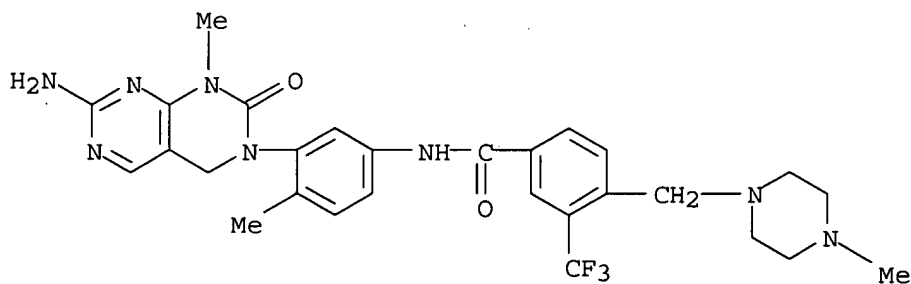
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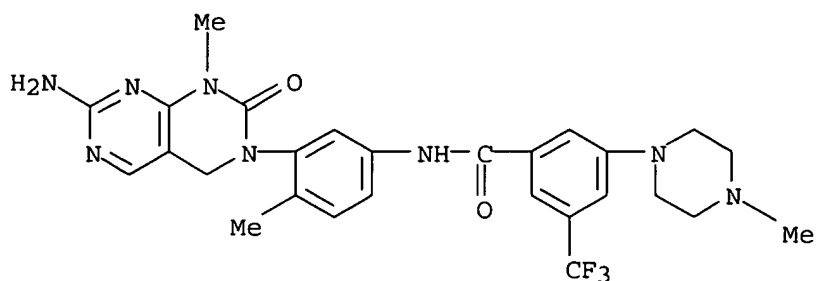
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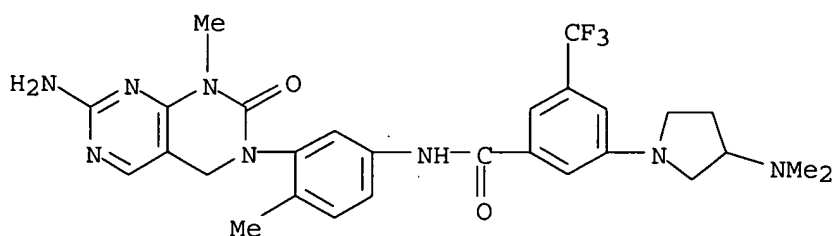
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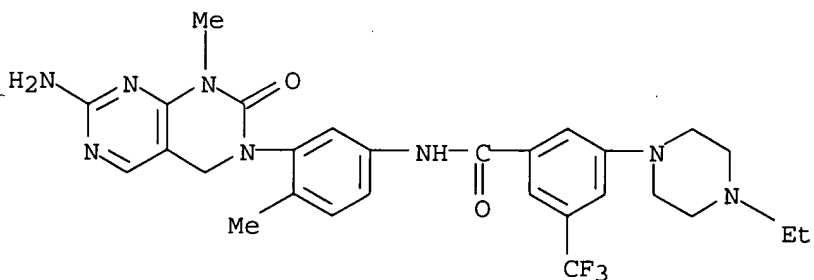
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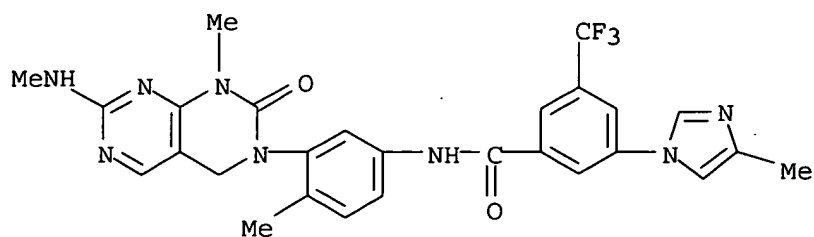
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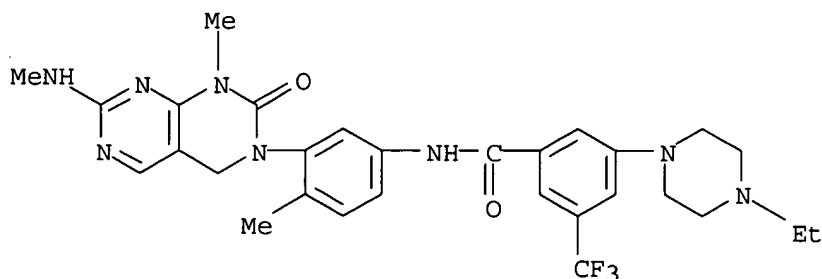
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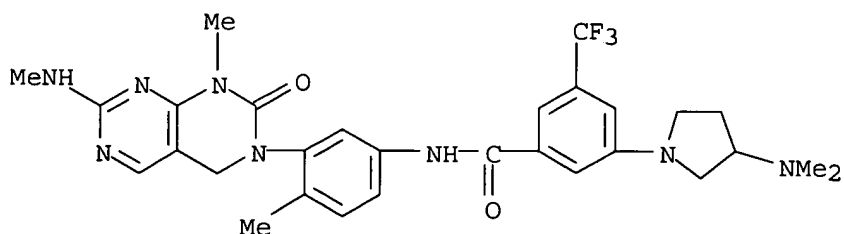
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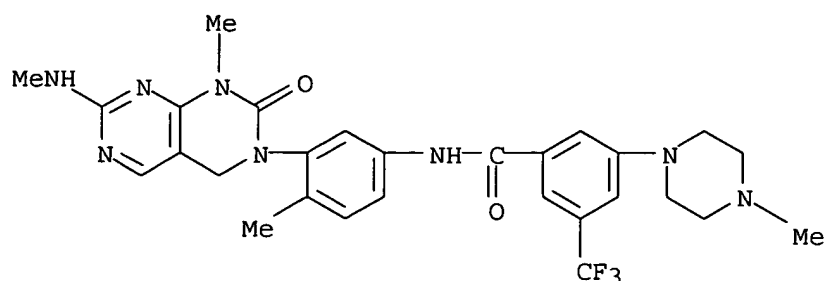
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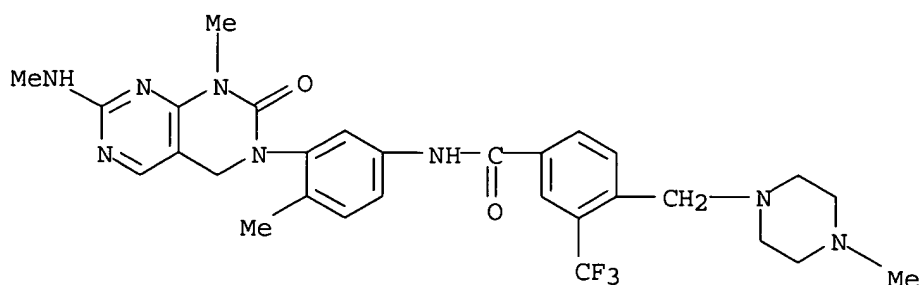
RN 839707-86-7 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(4-methyl-1-piperazinyl)-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)



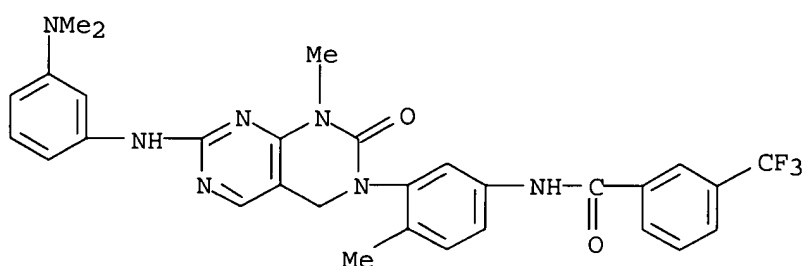
RN 839707-87-8 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



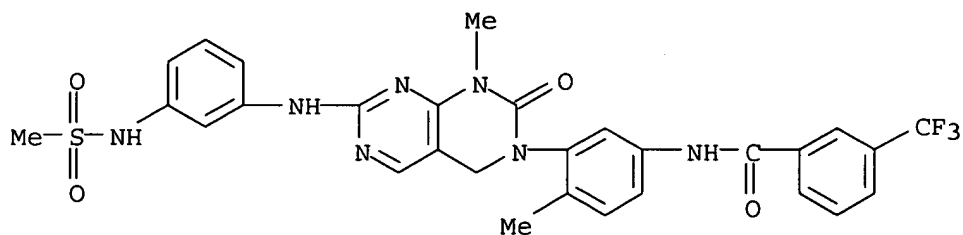
RN 839708-01-9 HCAPLUS

CN Benzamide, N-[3-[7-[[3-(dimethylamino)phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839708-02-0 HCAPLUS

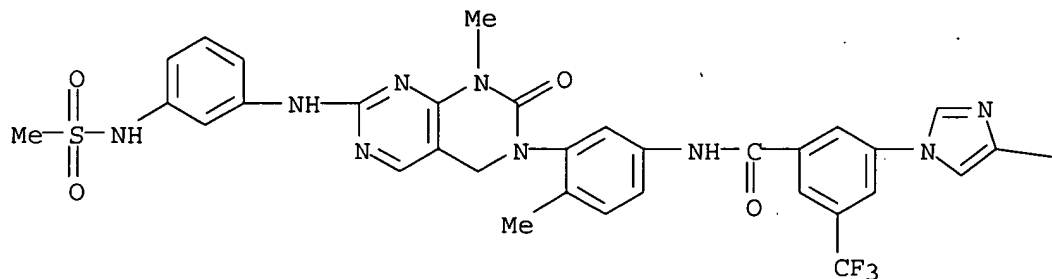
CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[3-[(methanesulfonyl)amino]phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839708-03-1 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[3-[(methanesulfonyl)amino]phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(4-methyl-1H-imidazol-1-yl)-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

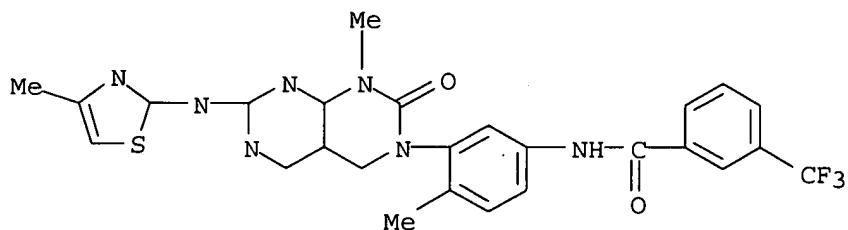


PAGE 1-B

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RN 839708-08-6 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[(4-methyl-2-thiazolyl)amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

IT 839708-09-7P 839708-10-0P 839708-11-1P

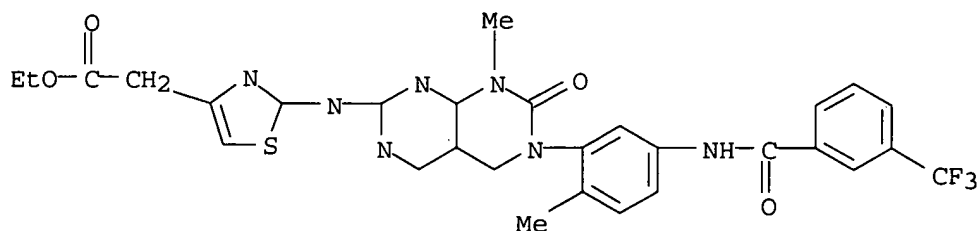
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 839708-26-8P 839708-27-9P 839708-28-0P
 839708-29-1P 839708-30-4P 839708-31-5P
 839708-32-6P 839708-33-7P 839708-34-8P
 839708-35-9P 839708-36-0P 839708-37-1P
 839708-38-2P 839708-39-3P 839708-40-6P
 839708-41-7P 839708-42-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrimidopyrimidines as protein kinase inhibitors)

RN 839708-09-7 HCAPLUS

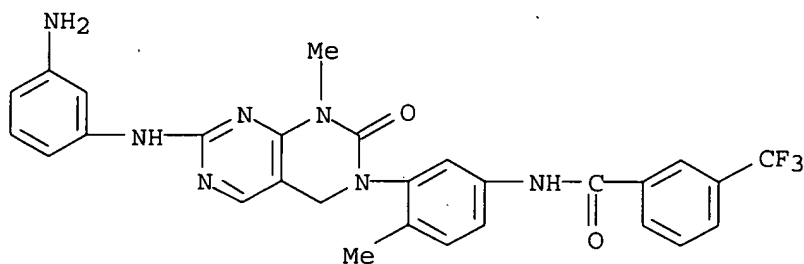
CN 4-Thiazoleacetic acid, 2-[[[5,6,7,8-tetrahydro-8-methyl-6-[2-methyl-5-[[3-(trifluoromethyl)benzoyl]amino]phenyl]-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

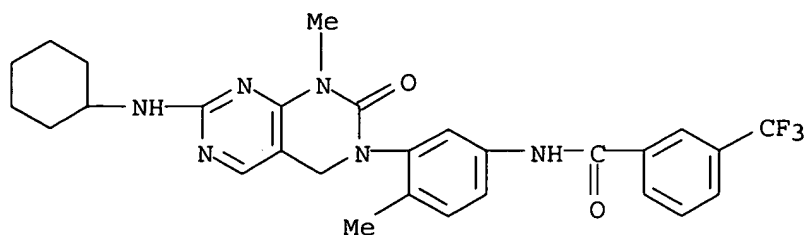
RN 839708-10-0 HCAPLUS

CN Benzamide, N-[3-[7-[(3-aminophenyl)amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



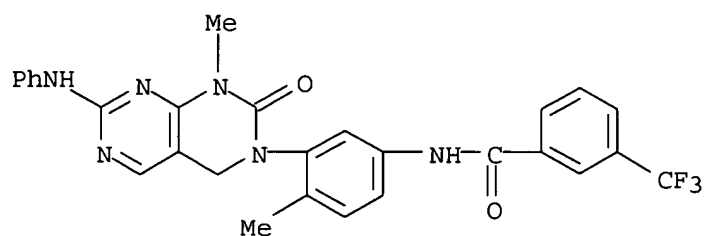
RN 839708-11-1 HCAPLUS

CN Benzamide, N-[3-[7-(cyclohexylamino)-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



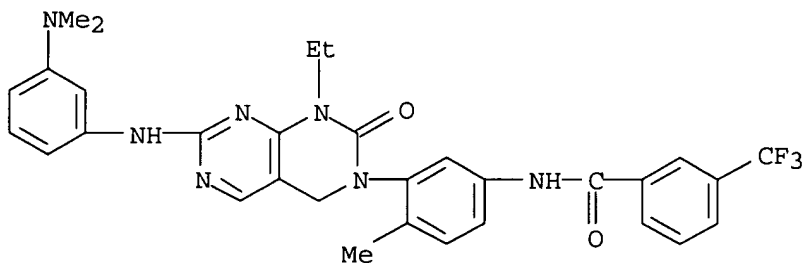
RN 839708-13-3 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



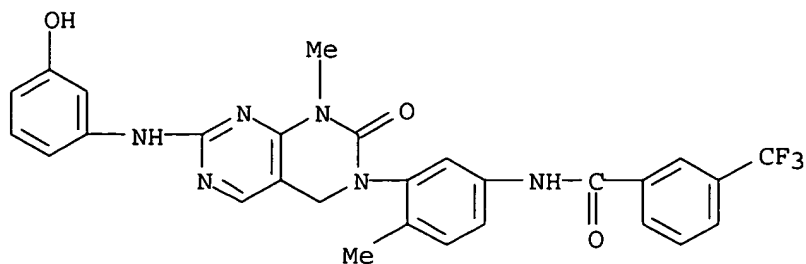
RN 839708-17-7 HCAPLUS

CN Benzamide, N-[3-[7-[[3-(dimethylamino)phenyl]amino]-1-ethyl-1,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



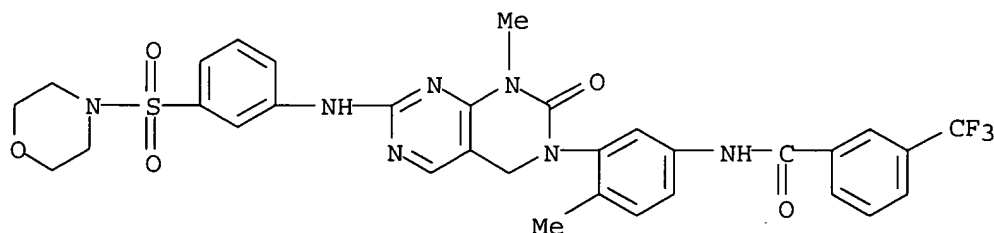
RN 839708-22-4 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-7-[(3-hydroxyphenyl)amino]-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



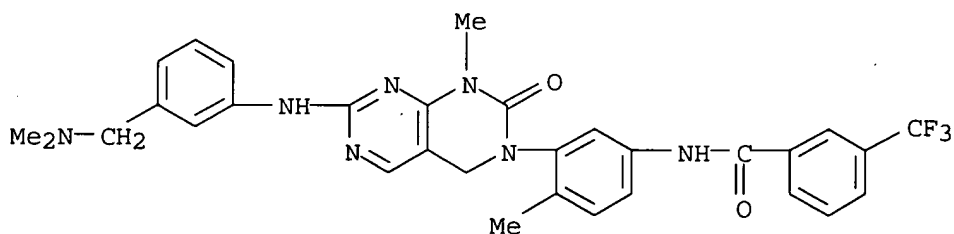
RN 839708-23-5 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[3-(4-morpholinylsulfonyl)phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839708-24-6 HCAPLUS

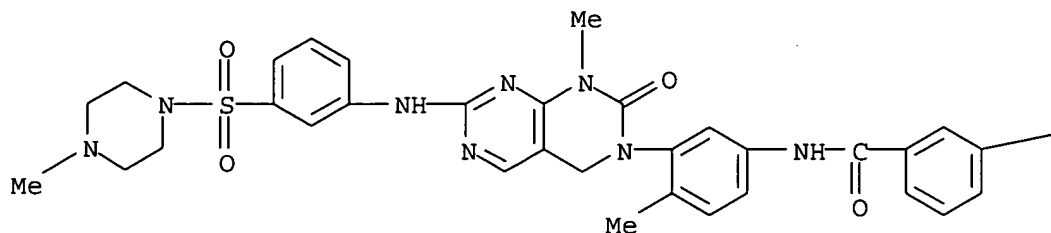
CN Benzamide, N-[3-[7-[[3-[(dimethylamino)methyl]phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839708-25-7 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[3-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

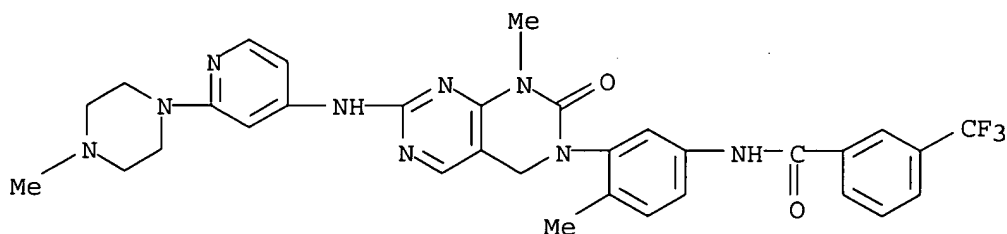


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RN 839708-26-8 HCAPLUS

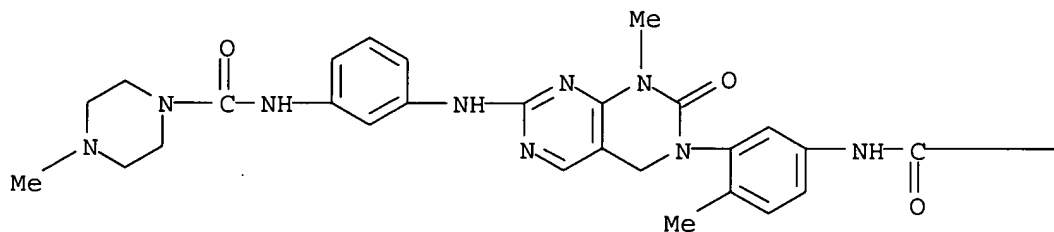
CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[2-(4-methyl-1-piperazinyl)-4-pyridinyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



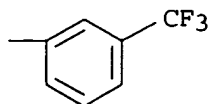
RN 839708-27-9 HCAPLUS

CN 1-Piperazinecarboxamide, 4-methyl-N-[3-[[5,6,7,8-tetrahydro-8-methyl-6-[2-methyl-5-[[3-(trifluoromethyl)benzoyl]amino]phenyl]-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]phenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



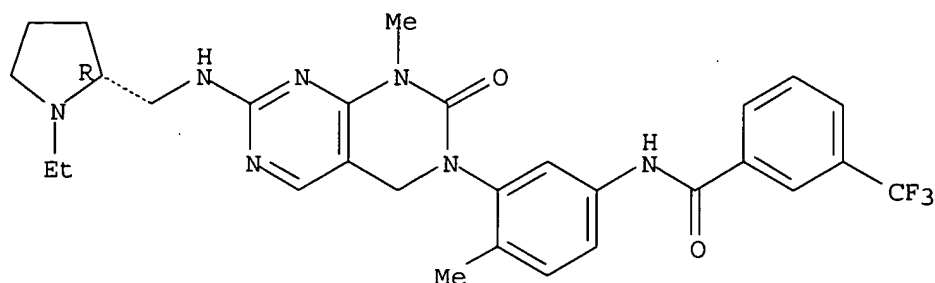
PAGE 1-B



RN 839708-28-0 HCAPLUS

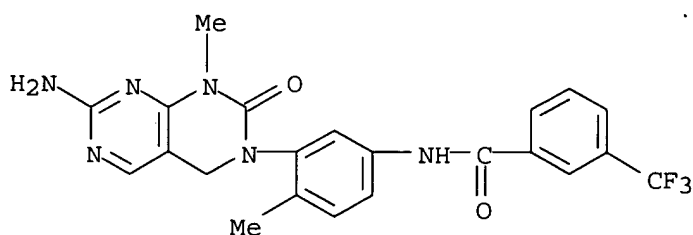
CN Benzamide, N-[3-[7-[[[(2R)-1-ethyl-2-pyrrolidinyl]methyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



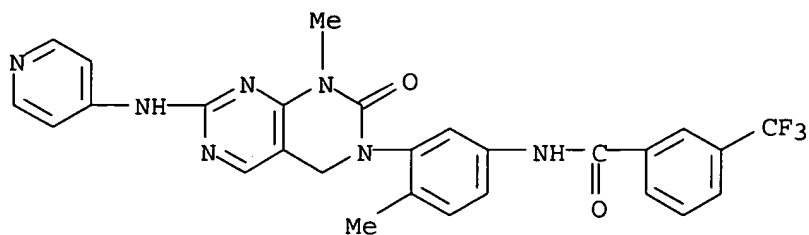
RN 839708-29-1 HCAPLUS

CN Benzamide, N-[3-(7-amino-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl)-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



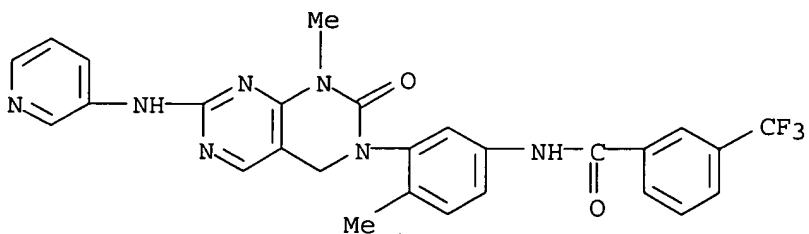
RN 839708-30-4 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-(4-pyridinylamino)pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



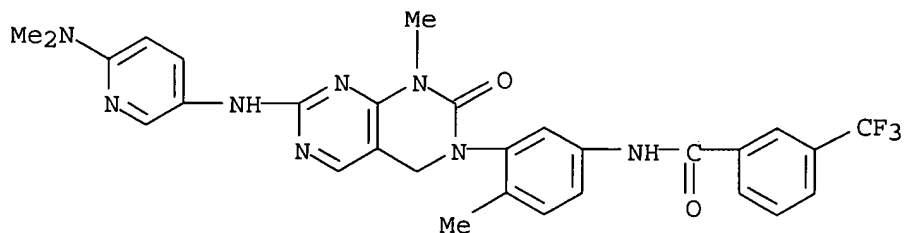
RN 839708-31-5 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-(3-pyridinylamino)pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839708-32-6 HCAPLUS

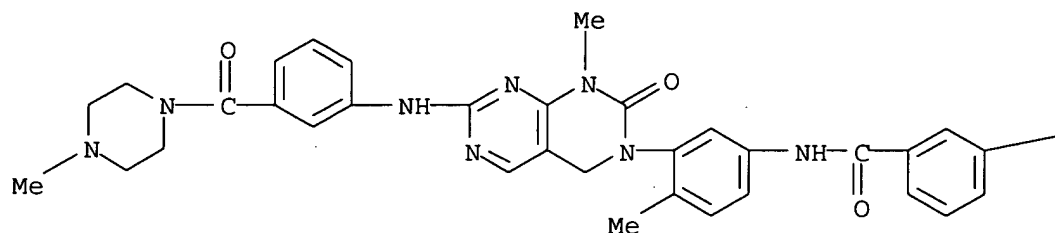
CN Benzamide, N-[3-[7-[[6-(dimethylamino)-3-pyridinyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839708-33-7 HCAPLUS

CN Benzamide, N-[3-[1,4-dihydro-1-methyl-7-[[3-[(4-methyl-1-piperazinyl)carbonyl]phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

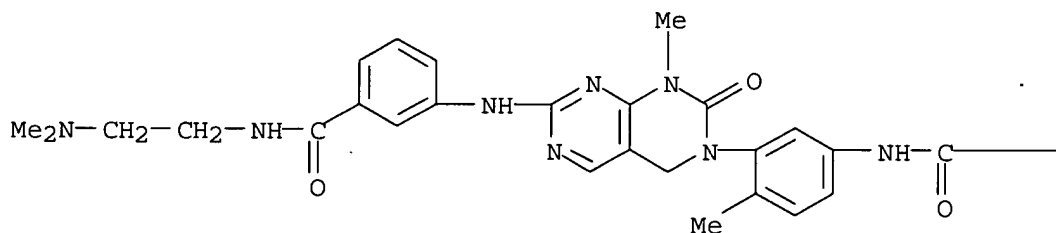


PAGE 1-B

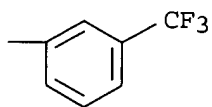
—CF₃

RN 839708-34-8 HCAPLUS
 CN Benzamide, N-[3-[7-[[3-[[[2-(dimethylamino)ethyl]amino]carbonyl]phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

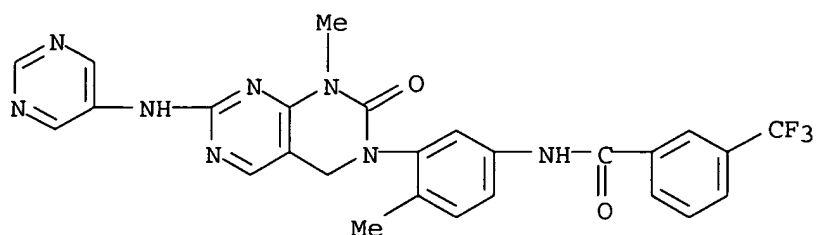
PAGE 1-A



PAGE 1-B

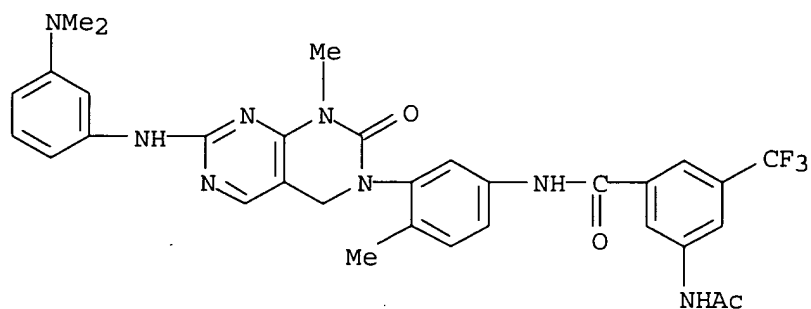


RN 839708-35-9 HCAPLUS
 CN Benzamide, N-[3-[1,4-dihydro-1-methyl-2-oxo-7-(5-pyrimidinylamino)pyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



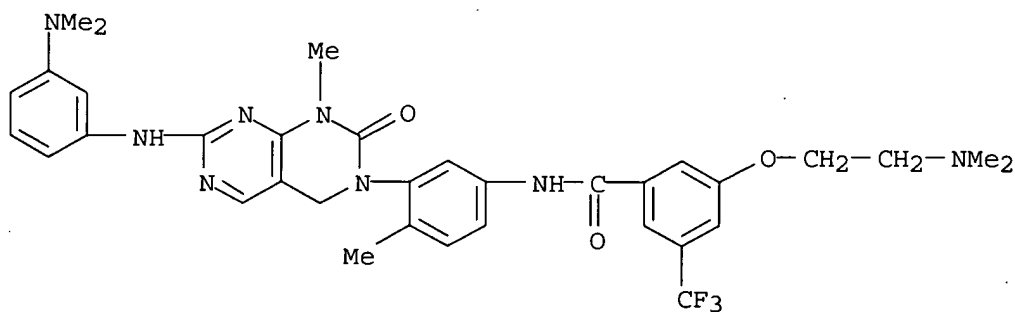
RN 839708-36-0 HCAPLUS

CN Benzamide, 3-(acetylamino)-N-[3-[7-[[3-(dimethylamino)phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839708-37-1 HCAPLUS

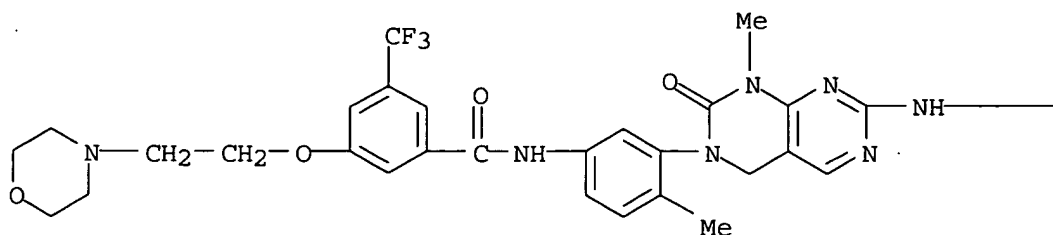
CN Benzamide, 3-[2-(dimethylamino)ethoxy]-N-[3-[7-[[3-(dimethylamino)phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)



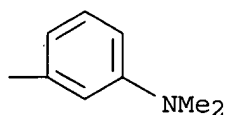
RN 839708-38-2 HCAPLUS

CN Benzamide, N-[3-[7-[[3-(dimethylamino)phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-[2-(4-morpholinyl)ethoxy]-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

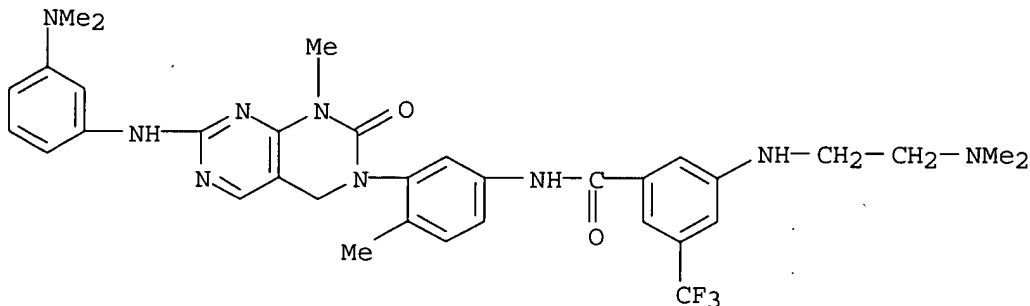


PAGE 1-B



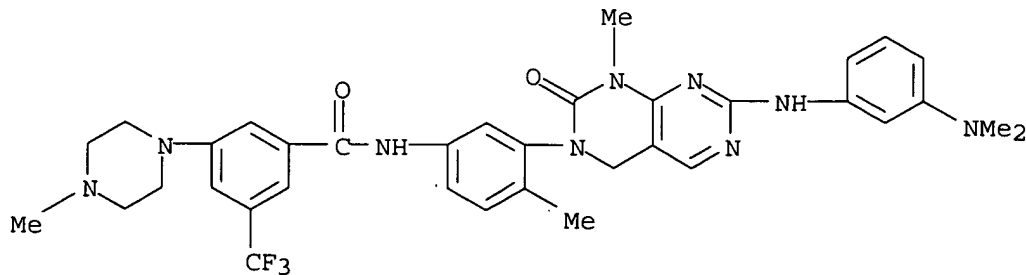
RN 839708-39-3 HCAPLUS

CN Benzamide, 3-[[2-(dimethylamino)ethyl]amino]-N-[3-[7-[[3-(dimethylamino)phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)



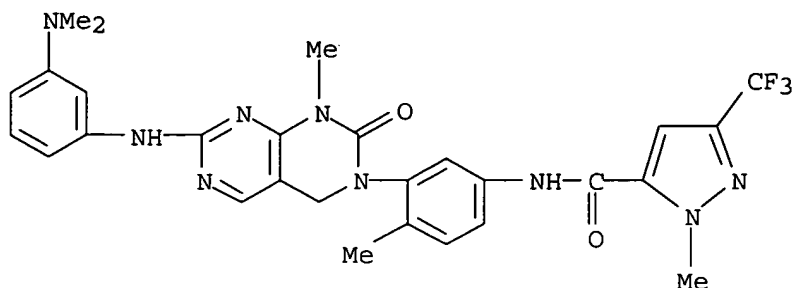
RN 839708-40-6 HCAPLUS

CN Benzamide, N-[3-[7-[[3-(dimethylamino)phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(4-methyl-1-piperazinyl)-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)



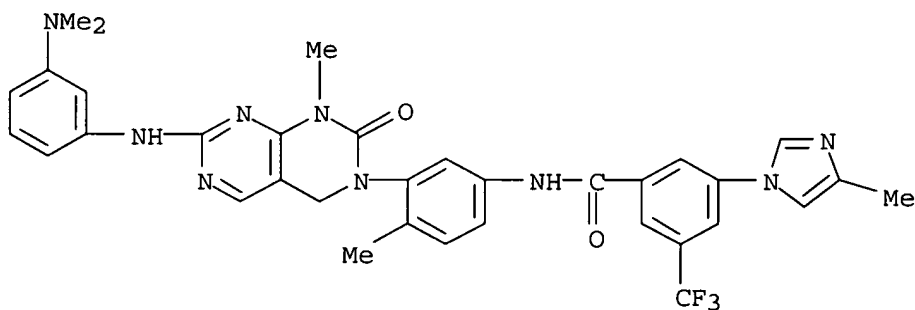
RN 839708-41-7 HCAPLUS

CN 1H-Pyrazole-5-carboxamide, N-[3-[7-[[3-(dimethylamino)phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-1-methyl-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 839708-42-8 HCAPLUS

CN Benzamide, N-[3-[7-[[3-(dimethylamino)phenyl]amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-4-methylphenyl]-3-(4-methyl-1H-imidazol-1-yl)-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)



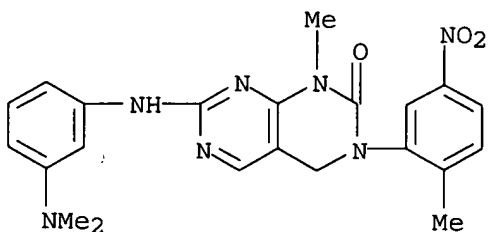
IT 839708-47-3P 839708-48-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyrimidopyrimidines as protein kinase inhibitors)

RN 839708-47-3 HCAPLUS

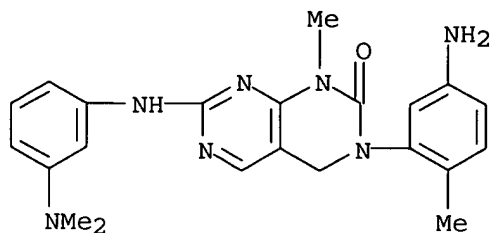
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[3-(dimethylamino)phenyl]amino]-3,4-dihydro-1-methyl-3-(2-methyl-5-nitrophenyl)- (9CI) (CA INDEX NAME)



RN 839708-48-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(5-amino-2-methylphenyl)-7-[[3-

(dimethylamino)phenyl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



L27 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:857176 HCAPLUS

DOCUMENT NUMBER: 141:350187

TITLE: Preparation of pyrimido compounds having antiproliferative activity

INVENTOR(S): Chen, Yi; Dermatakis, Apostolos; Liu, Jin-jun; Luk, Kin-chun; Michoud, Christophe; Rossman, Pamela Loreen

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 55 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2004204427 | A1 | 20041014 | US 2004-817697 | 20040402 |
| WO 2004089955 | A1 | 20041021 | WO 2004-EP3447 | 20040401 |

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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-461694P P 20030410

OTHER SOURCE(S): MARPAT 141:350187

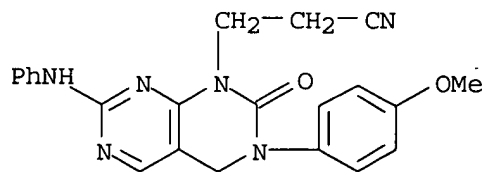
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

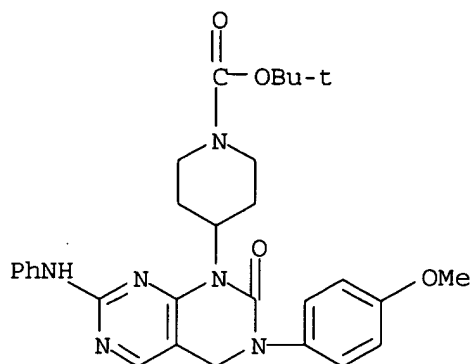
AB Disclosed are methods for preparing novel pyrimido compds. I [R1 = H, (un)substituted-alkyl, -cycloalkyl, -alkynyl, etc.; R2 and R3 independently = H, halo, (un)substituted-alkyl, -alkenyl, etc.; R4-8 independently = H, hydroxyalkyl, alkoxyalkyl, halo, etc.] that are selective inhibitors of both KDR and FGFR kinases. Thus, e.g., II was prepd via acylation of trans-4-(tert-butyldimethylsilanyloxy)cyclohexylami

ne (preparation given) with phosgene and subsequent cyclization with (2,4-dichloropyrimidin-5-ylmethyl)(4-methoxyphenyl)amine followed by desilylation. The IC50 values for I were as follows: KDR less than 0.50 μ M; FGFR less than 2 μ M. These compds. and their pharmaceutically acceptable salts are anti-proliferative agents useful in the treatment or control of solid tumors, in particular breast, colon, lung and prostate tumors. Also disclosed are pharmaceutical compns. containing these compds. and methods of treating cancer.

- IT **774232-16-5P**, 3-[3-(4-Methoxyphenyl)-2-oxo-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-1-yl]propionitrile
774232-32-5P, 4-[3-(4-Methoxyphenyl)-2-oxo-7-phenylamino-3,4-dihydro-2H-pyrimido[4,5-d]pyrimidin-1-yl]piperidine-1-carboxylic acid tert-butyl ester **774232-33-6P**, trans-1-[4-(tert-Butyldimethylsilyloxy)cyclohexyl]-3-(4-methoxyphenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-34-7P**, 3-[3-(4-Methoxyphenyl)-2-oxo-7-phenylamino-3,4-dihydro-2H-pyrimido[4,5-d]pyrimidin-1-yl]piperidine-1-carboxylic acid tert-butyl ester **774232-35-8P**, cis-1-[3-(tert-Butyldimethylsilyloxy)cyclopentyl]-3-(4-methoxyphenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-44-9P 774232-45-0P 774232-50-7P 774232-55-2P 774232-58-5P 774232-60-9P 774232-61-0P 774232-62-1P 774232-63-2P 774232-64-3P 774232-68-7P 774232-71-2P**
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (drug candidate; preparation of pyrimido[4,5-d]pyrimidinones as selective inhibitors of both KDR and FGFR kinases)
 RN **774232-16-5 HCAPLUS**
 CN Pyrimido[4,5-d]pyrimidine-1(2H)-propanenitrile, 3,4-dihydro-3-(4-methoxyphenyl)-2-oxo-7-(phenylamino)- (9CI) (CA INDEX NAME)



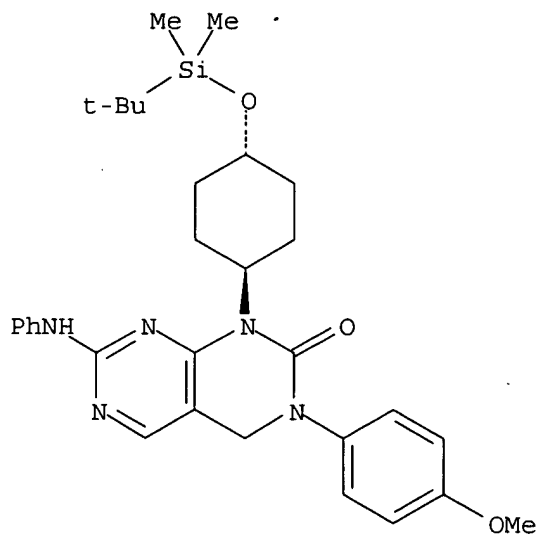
- RN **774232-32-5 HCAPLUS**
 CN 1-Piperidinecarboxylic acid, 4-[3,4-dihydro-3-(4-methoxyphenyl)-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 774232-33-6 HCAPLUS

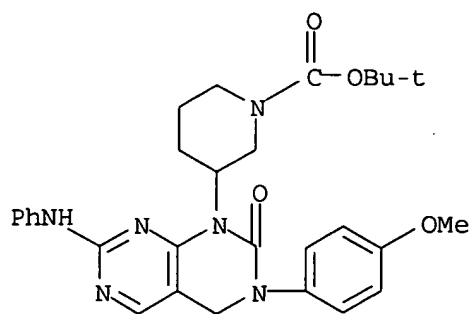
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[trans-4-[[[1,1-dimethylethyl]dimethylsilyl]oxy]cyclohexyl]-3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 774232-34-7 HCAPLUS

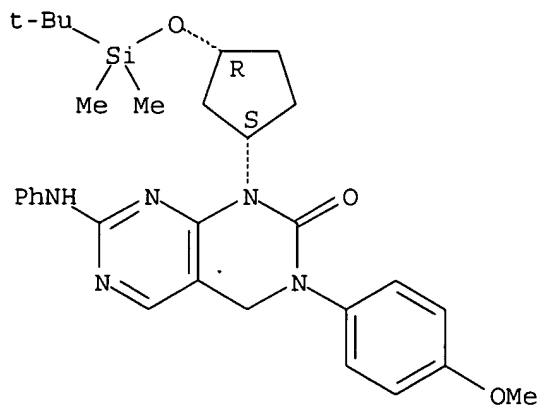
CN 1-Piperidinecarboxylic acid, 3-[3,4-dihydro-3-(4-methoxyphenyl)-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 774232-35-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1R,3S)-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]cyclopentyl]-3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino)-, rel- (9CI) (CA INDEX NAME)

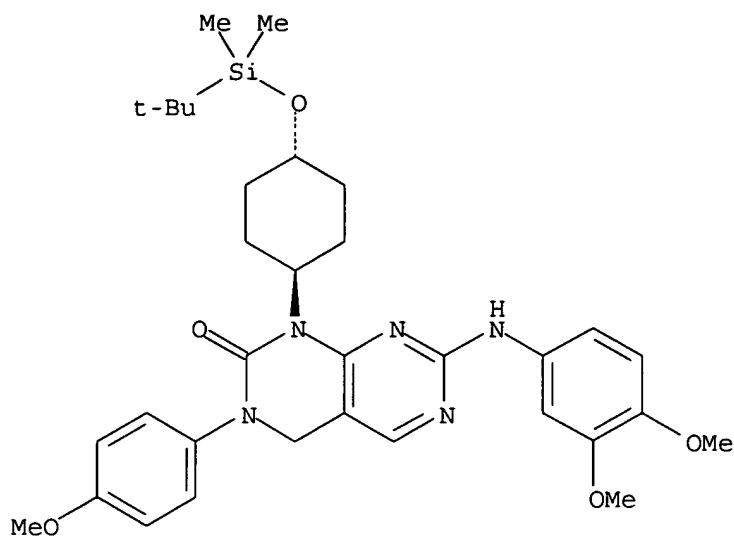
Relative stereochemistry.



RN 774232-44-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(3,4-dimethoxyphenyl)amino]-1-[[trans-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]cyclohexyl]-3,4-dihydro-3-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

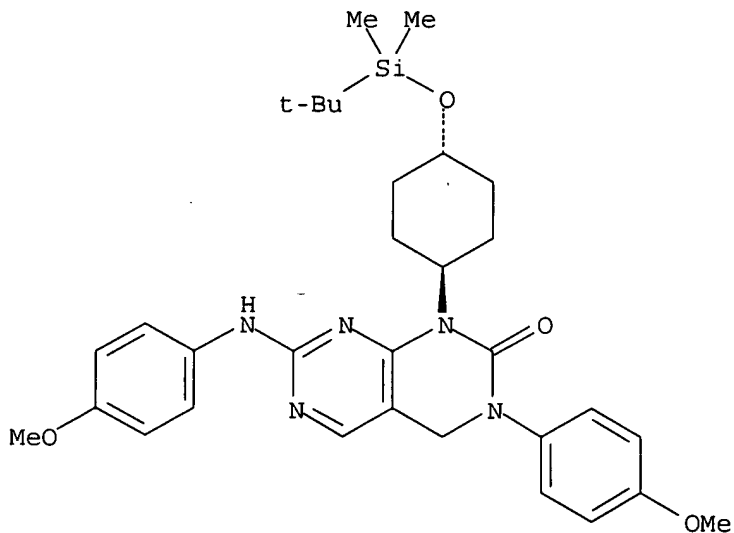
Relative stereochemistry.



RN 774232-45-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[trans-4-[[[1,1-dimethylethyl)dimethylsilyl]oxy]cyclohexyl]-3,4-dihydro-3-(4-methoxyphenyl)-7-[(4-methoxyphenyl)amino]- (9CI) (CA INDEX NAME)

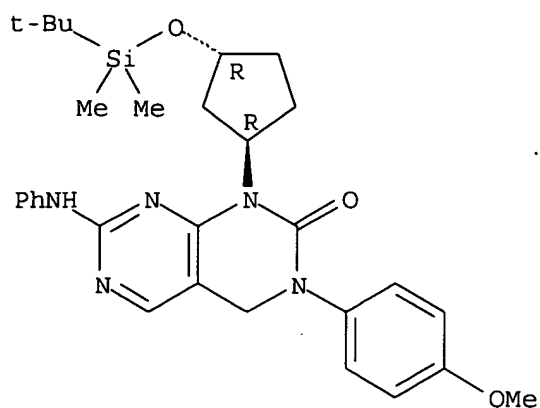
Relative stereochemistry.



RN 774232-50-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1R,3R)-3-[[[1,1-dimethylethyl)dimethylsilyl]oxy]cyclopentyl]-3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino)-, rel- (9CI) (CA INDEX NAME)

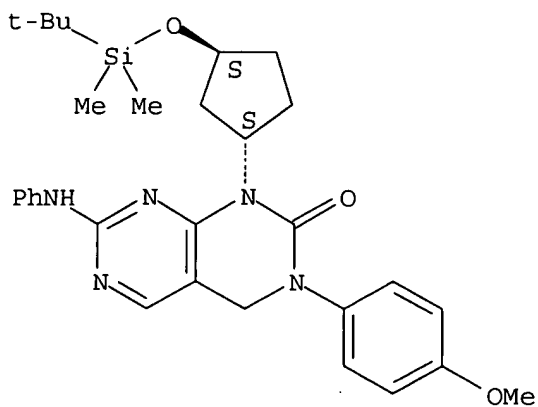
Absolute stereochemistry. Rotation (-).



RN 774232-55-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1S,3S)-3-[[[1,1-dimethylethyl]dimethylsilyl]oxy]cyclopentyl]-3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino)- (9CI) (CA INDEX NAME)

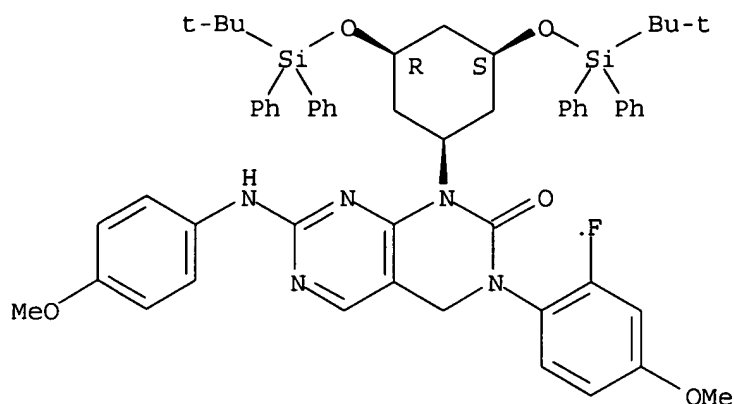
Absolute stereochemistry. Rotation (-).



RN 774232-58-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1 α ,3 α ,5 α)-3,5-bis[[[1,1-dimethylethyl]diphenylsilyl]oxy]cyclohexyl]-3-(2-fluoro-4-methoxyphenyl)-3,4-dihydro-7-[(4-methoxyphenyl)amino]- (9CI) (CA INDEX NAME)

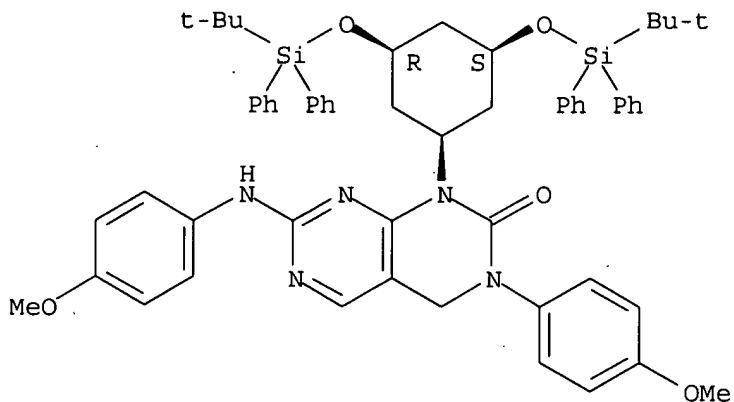
Relative stereochemistry.



RN 774232-60-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1 α ,3 α ,5 α)-3,5-bis[[[(1,1-dimethylethyl)diphenylsilyl]oxy]cyclohexyl]-3,4-dihydro-3-(4-methoxyphenyl)-7-[(4-methoxyphenyl)amino]- (9CI) (CA INDEX NAME)

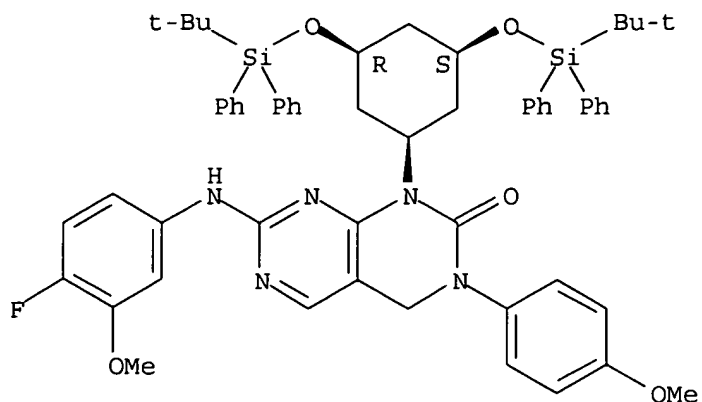
Relative stereochemistry.



RN 774232-61-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1 α ,3 α ,5 α)-3,5-bis[[[(1,1-dimethylethyl)diphenylsilyl]oxy]cyclohexyl]-7-[(4-fluoro-3-methoxyphenyl)amino]-3,4-dihydro-3-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

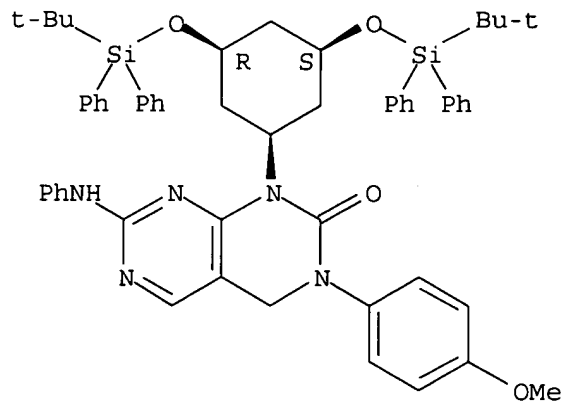
Relative stereochemistry.



RN 774232-62-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1 α ,3 α ,5 α)-3,5-bis[[[(1,1-dimethylethyl)diphenylsilyl]oxy]cyclohexyl]-3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino)- (9CI) (CA INDEX NAME)

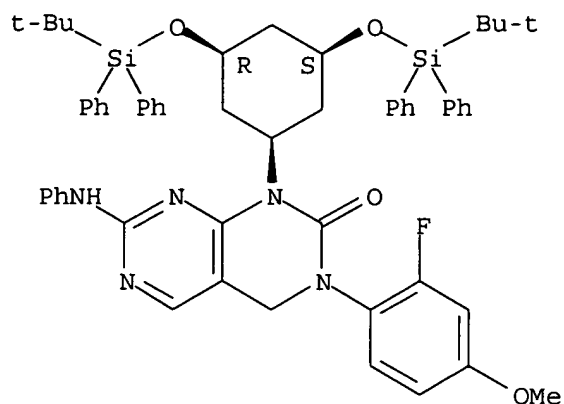
Relative stereochemistry.



RN 774232-63-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1 α ,3 α ,5 α)-3,5-bis[[[(1,1-dimethylethyl)diphenylsilyl]oxy]cyclohexyl]-3-(2-fluoro-4-methoxyphenyl)-3,4-dihydro-7-(phenylamino)- (9CI) (CA INDEX NAME)

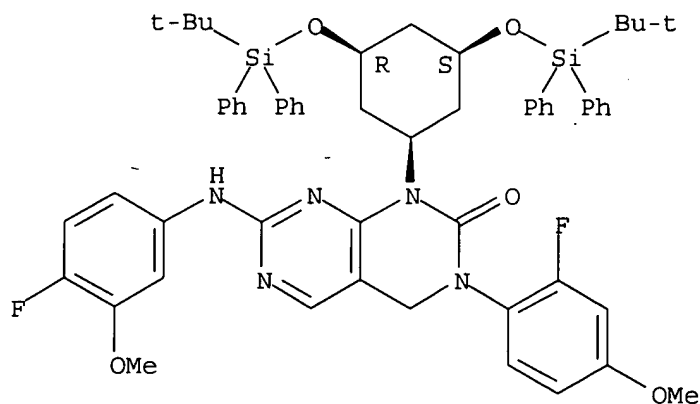
Relative stereochemistry.



RN 774232-64-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1 α ,3 α ,5 α)-3,5-bis[[[(1,1-dimethylethyl)diphenylsilyl]oxy]cyclohexyl]-3-(2-fluoro-4-methoxyphenyl)-7-[(4-fluoro-3-methoxyphenyl)amino]-3,4-dihydro- (9CI) (CA INDEX NAME)

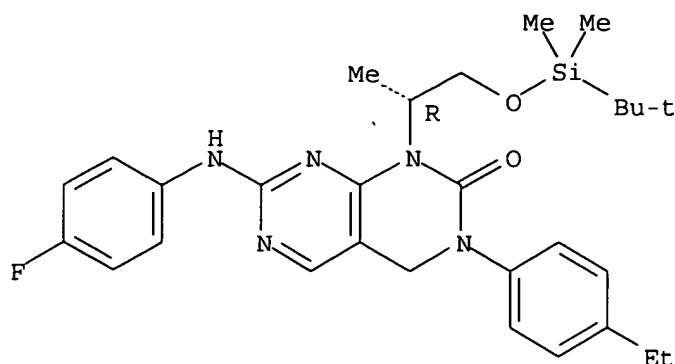
Relative stereochemistry.



RN 774232-68-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1R)-2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-methylethyl]-3-(4-ethylphenyl)-7-[(4-fluorophenyl)amino]-3,4-dihydro- (9CI) (CA INDEX NAME)

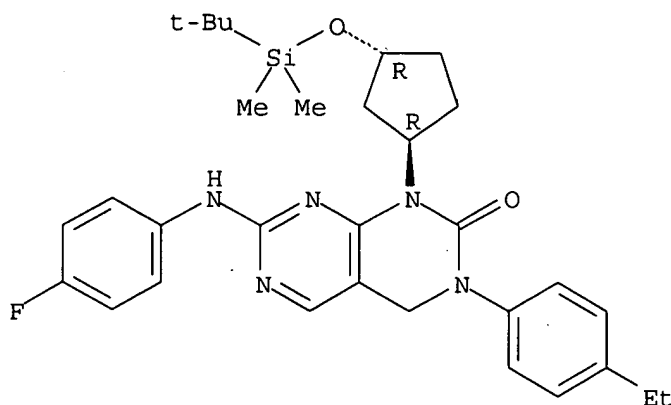
Absolute stereochemistry.



RN 774232-71-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1R,3R)-3-[(1,1-dimethylethyl)dimethylsilyloxy]cyclopentyl]-3-(4-ethylphenyl)-7-[(4-fluorophenyl)amino]-3,4-dihydro-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



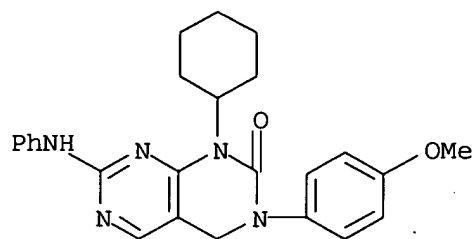
IT **774231-91-3P**, 1-Cyclohexyl-3-(4-methoxyphenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774231-92-4P**, 3-(4-Methoxyphenyl)-7-phenylamino-1-piperidin-4-yl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774231-93-5P**, 1-(trans-4-Hydroxycyclohexyl)-3-(4-methoxyphenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774231-94-6P**, 3-(4-Methoxyphenyl)-7-phenylamino-1-piperidin-3-yl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774231-95-7P**, 1-Cyclopentyl-3-(4-methoxyphenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774231-96-8P**, 1-(1,1-Dioxo-tetrahydrothiophen-3-yl)-3-(4-methoxyphenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774231-97-9P**, 3-[3-(4-Methoxyphenyl)-2-oxo-7-phenylamino-3,4-dihydro-2H-pyrimido[4,5-d]pyrimidin-1-yl]piperidine-1-carboxaldehyde **774231-98-0P**, 3-(4-Methoxyphenyl)-7-phenylamino-1-(tetrahydro-pyran-4-yl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774231-99-1P**, 1-(trans-3-Hydroxycyclopentyl)-3-(4-methoxyphenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-00-7P**, 1-(cis-3-Hydroxycyclopentyl)-3-(4-methoxyphenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-01-8P**,

(R)-3-(4-Methoxyphenyl)-7-phenylamino-1-(tetrahydrofuran-3-yl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-02-9P**,
 (R)-3-(4-Methoxyphenyl)-7-phenylamino-1-(pyrrolidin-3-yl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-03-0P**,
 trans-7-(4-Fluorophenylamino)-1-(3-hydroxycyclopentyl)-3-(4-methoxyphenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-04-1P**,
 trans-3-(2-Fluoro-4-methoxyphenyl)-1-(3-hydroxycyclopentyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-05-2P**,
 (S)-(+)-1-(2-Hydroxy-1-methylethyl)-3-(4-methoxyphenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-06-3P**,
 (S)-(+)-7-(4-Fluorophenylamino)-1-(2-hydroxy-1-methylethyl)-3-(4-methoxyphenyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-07-4P**, trans-3-(2-Fluoro-4-methoxyphenyl)-1-(4-hydroxycyclohexyl)-7-(4-methoxyphenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-08-5P**, trans-3-(2-Fluoro-4-methoxyphenyl)-1-(4-hydroxycyclohexyl)-7-(3,4-dimethoxyphenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-09-6P**, trans-3-(4-Methoxyphenyl)-1-(4-hydroxycyclohexyl)-7-(3,4-dimethoxyphenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-10-9P**, trans-3-(4-Methoxyphenyl)-1-(4-hydroxycyclohexyl)-7-(4-methoxyphenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-11-0P**, (S)-(+)-3-(2-Fluoro-4-methoxyphenyl)-7-(4-fluorophenylamino)-1-(2-hydroxy-1-methylethyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-12-1P**, (S)-(+)-3-(2-Fluoro-4-methoxyphenyl)-1-(2-hydroxy-1-methylethyl)-7-(4-methoxyphenylamino)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-13-2P**, (R)-(-)-1-(2-Hydroxy-1-methylethyl)-3-(4-methoxyphenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-14-3P**, 3-(4-Methoxyphenyl)-1-methyl-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-15-4P**, 1-(2-Methoxyethoxymethyl)-3-(4-methoxyphenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-17-6P** **774232-18-7P**, (R)-1-(2-Hydroxypropyl)-3-(4-methoxyphenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-19-8P** **774232-21-2P**, 3-[3-(4-Methoxyphenyl)-2-oxo-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-1-yl]propionamide **774232-22-3P**, (S)-(+)-1-(2-Hydroxypropyl)-3-(4-methoxyphenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-23-4P** **774232-24-5P** **774232-25-6P** **774232-26-7P** **774232-27-8P** **774232-28-9P** **774232-29-0P**, (R)-3-(4-Ethylphenyl)-7-(4-fluorophenylamino)-1-(2-hydroxy-1-methylethyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-30-3P**, trans-3-(4-Ethylphenyl)-7-(4-fluorophenylamino)-1-(3-hydroxycyclopentyl)-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one **774232-31-4P**, 1-Cyclopropylmethyl-3-(4-methoxyphenyl)-7-phenylamino-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2-one
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

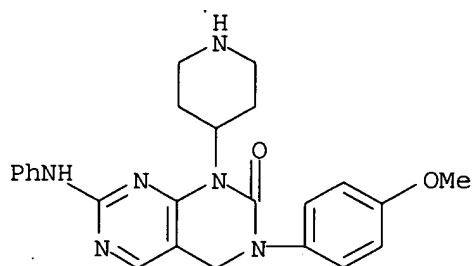
(drug candidate; preparation of pyrimido[4,5-d]pyrimidinones as selective inhibitors of both KDR and FGFR kinases)

RN 774231-91-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclohexyl-3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino)- (9CI) (CA INDEX NAME)

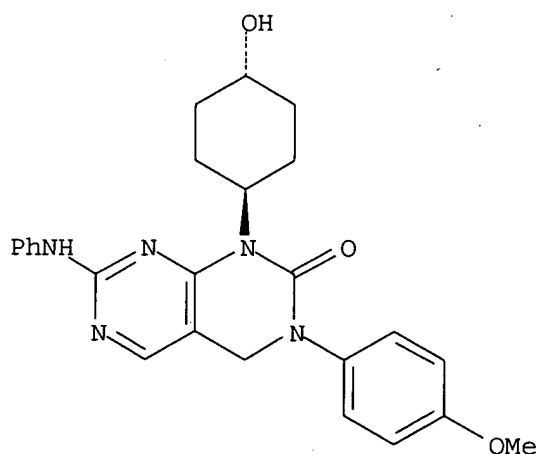


RN 774231-92-4 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino)-1-(4-piperidinyl)- (9CI) (CA INDEX NAME)

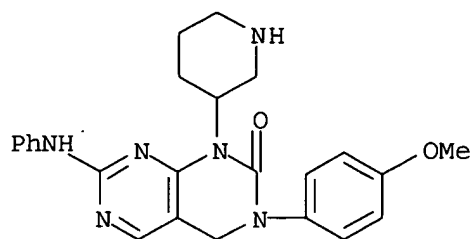


RN 774231-93-5 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-(trans-4-hydroxycyclohexyl)-3-(4-methoxyphenyl)-7-(phenylamino)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

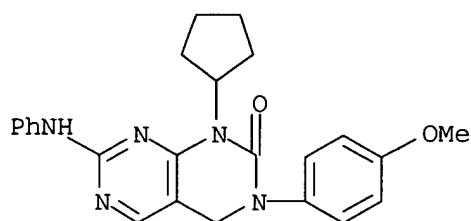


RN 774231-94-6 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino)-1-(3-piperidinyl)- (9CI) (CA INDEX NAME)



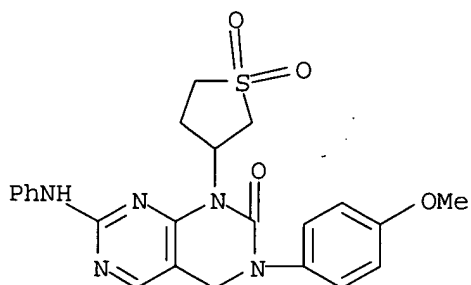
RN 774231-95-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino)- (9CI) (CA INDEX NAME)



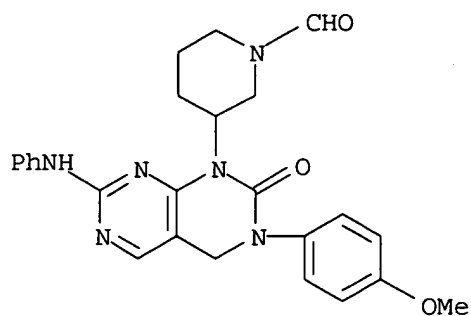
RN 774231-96-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino)-1-(tetrahydro-1,1-dioxido-3-thienyl)- (9CI) (CA INDEX NAME)



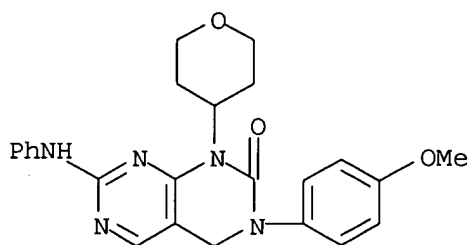
RN 774231-97-9 HCAPLUS

CN 1-Piperidinecarboxaldehyde, 3-[3,4-dihydro-3-(4-methoxyphenyl)-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]- (9CI) (CA INDEX NAME)



RN 774231-98-0 HCAPLUS

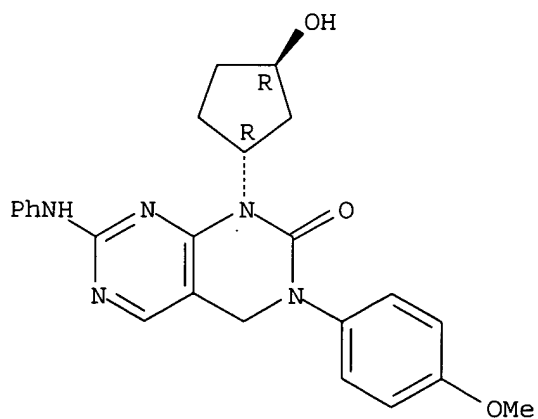
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino)-1-(tetrahydro-2H-pyran-4-yl)- (9CI) (CA INDEX NAME)



RN 774231-99-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-[(1R,3R)-3-hydroxycyclopentyl]-3-(4-methoxyphenyl)-7-(phenylamino)-, rel- (9CI) (CA INDEX NAME)

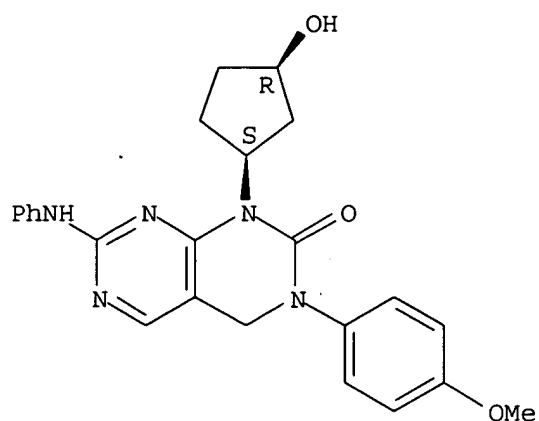
Relative stereochemistry.



RN 774232-00-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-[(1R,3S)-3-hydroxycyclopentyl]-3-(4-methoxyphenyl)-7-(phenylamino)-, rel- (9CI) (CA INDEX NAME)

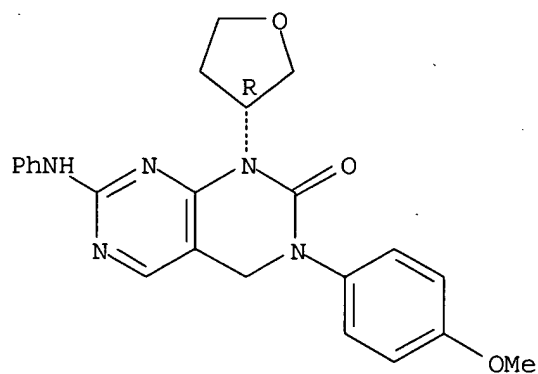
Relative stereochemistry.



RN 774232-01-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino)-1-[(3R)-tetrahydro-3-furanyl]- (9CI) (CA INDEX NAME)

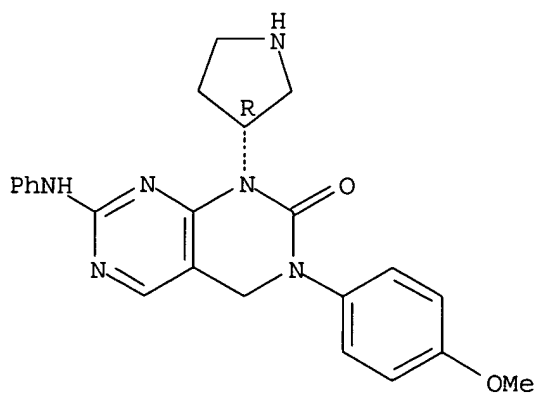
Absolute stereochemistry.



RN 774232-02-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino)-1-(3R)-3-pyrrolidinyl- (9CI) (CA INDEX NAME)

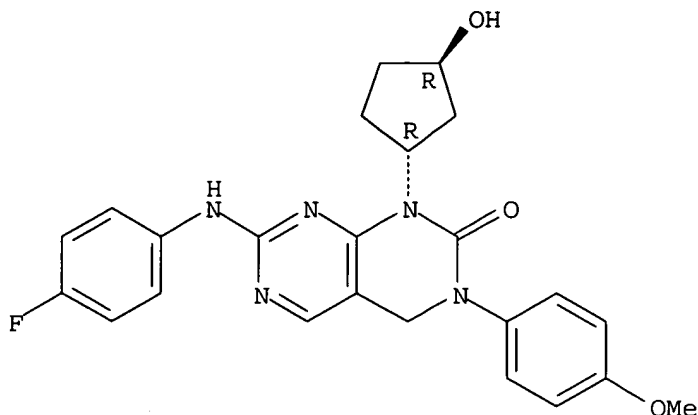
Absolute stereochemistry.



RN 774232-03-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(4-fluorophenyl)amino]-3,4-dihydro-1-[(1R,3R)-3-hydroxycyclopentyl]-3-(4-methoxyphenyl)-, rel- (9CI) (CA INDEX NAME)

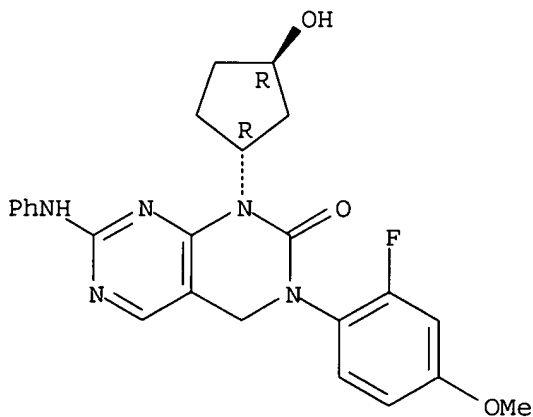
Relative stereochemistry.



RN 774232-04-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-fluoro-4-methoxyphenyl)-3,4-dihydro-1-[(1R,3R)-3-hydroxycyclopentyl]-7-(phenylamino)- (9CI) (CA INDEX NAME)

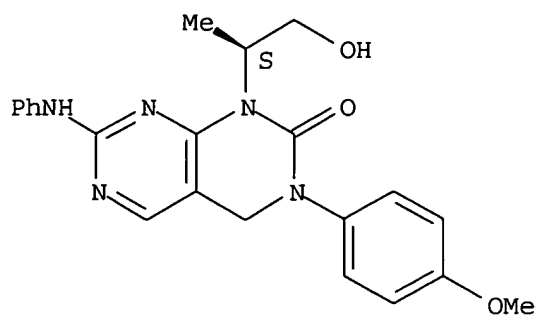
Relative stereochemistry.



RN 774232-05-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-[(1S)-2-hydroxy-1-methylethyl]-3-(4-methoxyphenyl)-7-(phenylamino)- (9CI) (CA INDEX NAME)

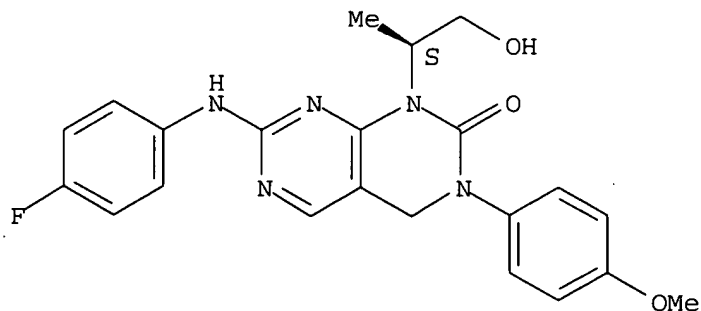
Absolute stereochemistry. Rotation (+).



RN 774232-06-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(4-fluorophenyl)amino]-3,4-dihydro-1-[(1S)-2-hydroxy-1-methylethyl]-3-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

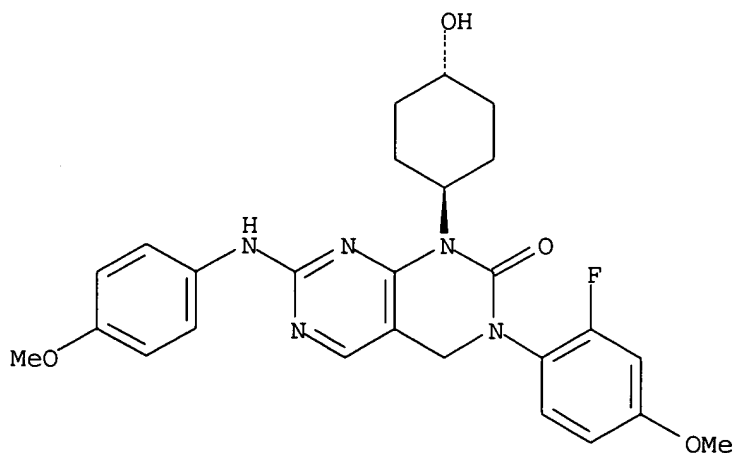
Absolute stereochemistry. Rotation (+).



RN 774232-07-4 HCAPLUS

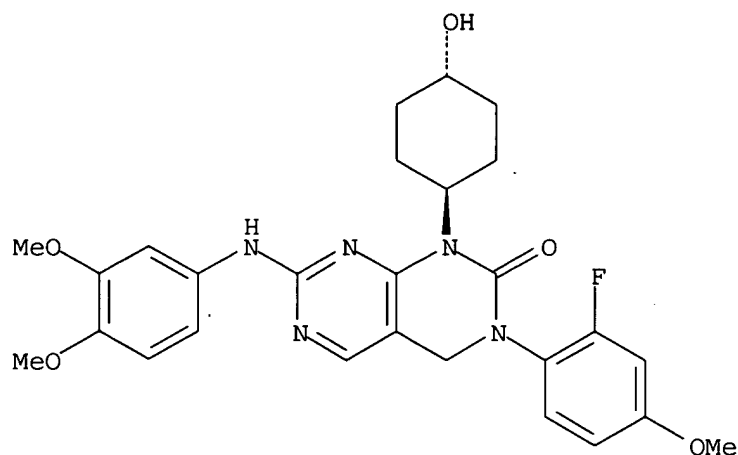
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-fluoro-4-methoxyphenyl)-3,4-dihydro-1-(trans-4-hydroxycyclohexyl)-7-[(4-methoxyphenyl)amino]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



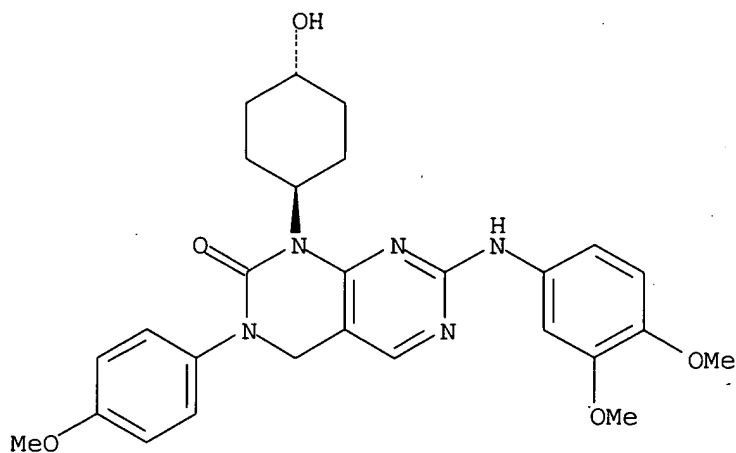
RN 774232-08-5 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(3,4-dimethoxyphenyl)amino]-3-(2-fluoro-4-methoxyphenyl)-3,4-dihydro-1-(trans-4-hydroxycyclohexyl)- (9CI)
 (CA INDEX NAME)

Relative stereochemistry.



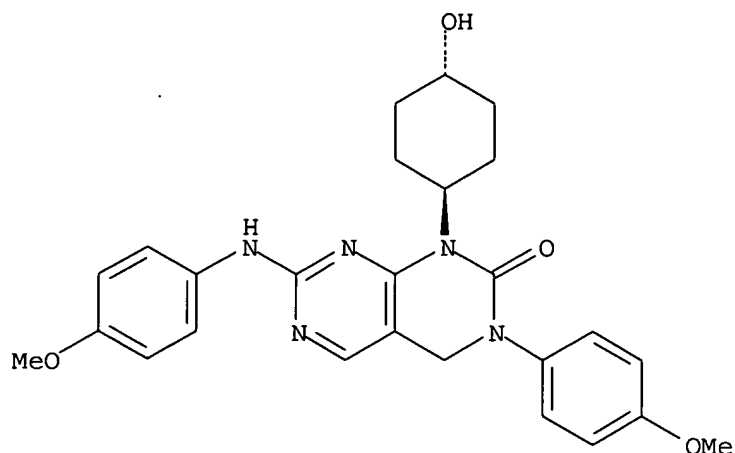
RN 774232-09-6 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(3,4-dimethoxyphenyl)amino]-3,4-dihydro-1-(trans-4-hydroxycyclohexyl)-3-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 774232-10-9 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-(trans-4-hydroxycyclohexyl)-3-(4-methoxyphenyl)-7-[(4-methoxyphenyl)amino]- (9CI)
 (CA INDEX NAME)

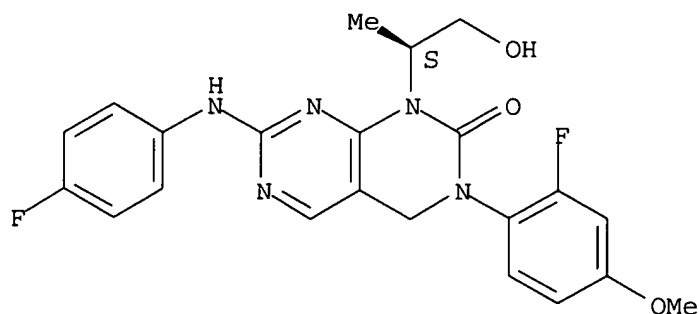
Relative stereochemistry.



RN 774232-11-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-fluoro-4-methoxyphenyl)-7-[(4-fluorophenyl)amino]-3,4-dihydro-1-[(1S)-2-hydroxy-1-methylethyl]- (9CI)
(CA INDEX NAME)

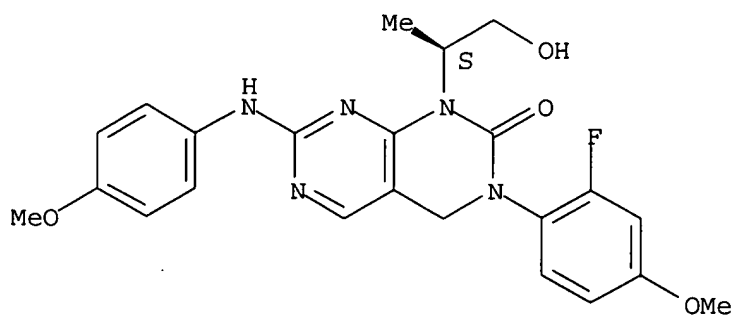
Absolute stereochemistry. Rotation (+).



RN 774232-12-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-fluoro-4-methoxyphenyl)-3,4-dihydro-1-[(1S)-2-hydroxy-1-methylethyl]-7-[(4-methoxyphenyl)amino]- (9CI)
(CA INDEX NAME)

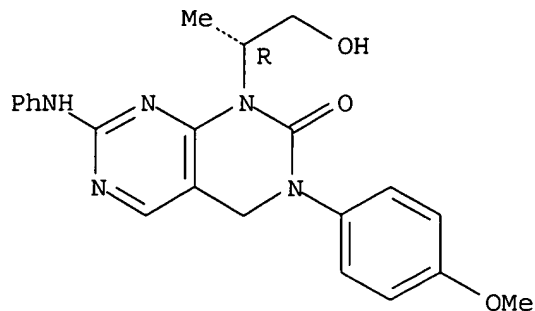
Absolute stereochemistry. Rotation (+).



RN 774232-13-2 HCAPLUS

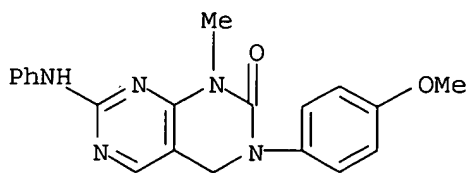
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-[(1R)-2-hydroxy-1-methylethyl]-3-(4-methoxyphenyl)-7-(phenylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



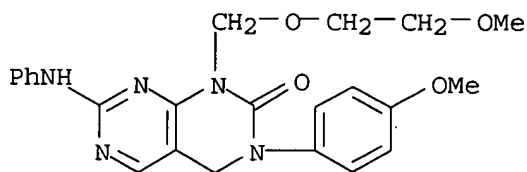
RN 774232-14-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-3-(4-methoxyphenyl)-1-methyl-7-(phenylamino)- (9CI) (CA INDEX NAME)



RN 774232-15-4 HCAPLUS

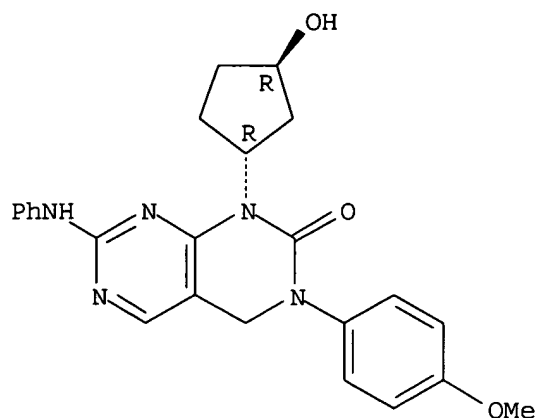
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-[(2-methoxyethoxy)methyl]-3-(4-methoxyphenyl)-7-(phenylamino)- (9CI) (CA INDEX NAME)



RN 774232-17-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-[(1R,3R)-3-hydroxycyclopentyl]-3-(4-methoxyphenyl)-7-(phenylamino)- (9CI) (CA INDEX NAME)

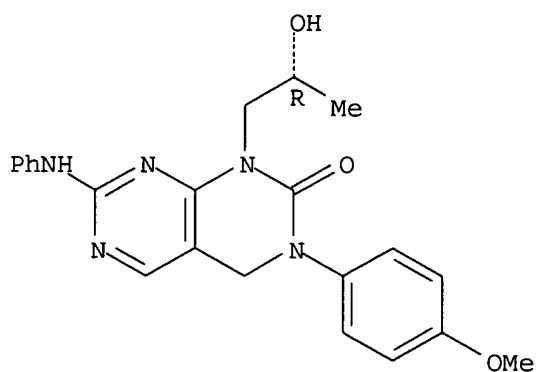
Absolute stereochemistry. Rotation (+).



RN 774232-18-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-[(2R)-2-hydroxypropyl]-3-(4-methoxyphenyl)-7-(phenylamino)- (9CI) (CA INDEX NAME)

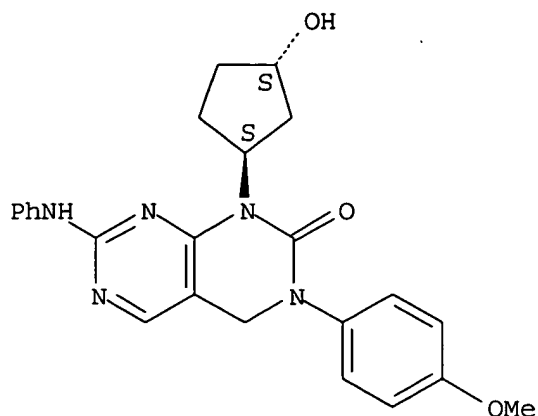
Absolute stereochemistry.



RN 774232-19-8 HCAPLUS

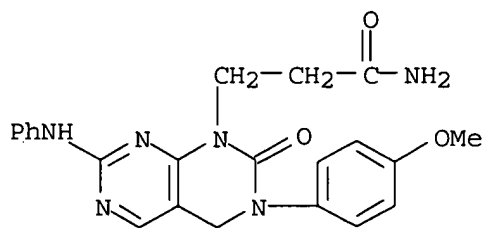
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-[(1S,3S)-3-hydroxycyclopentyl]-3-(4-methoxyphenyl)-7-(phenylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 774232-21-2 HCAPLUS

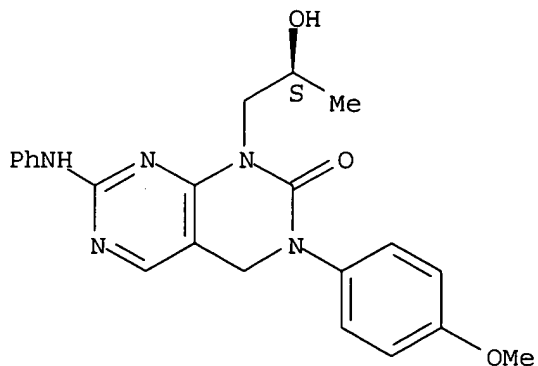
CN Pyrimido[4,5-d]pyrimidine-1(2H)-propanamide, 3,4-dihydro-3-(4-methoxyphenyl)-2-oxo-7-(phenylamino)- (9CI) (CA INDEX NAME)



RN 774232-22-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-[(2S)-2-hydroxypropyl]-3-(4-methoxyphenyl)-7-(phenylamino)- (9CI) (CA INDEX NAME)

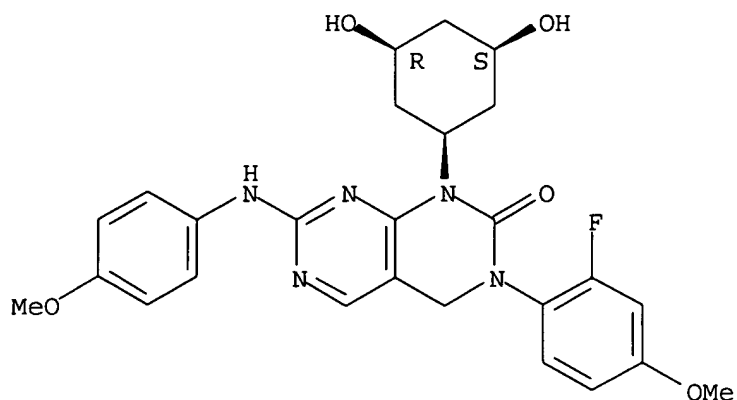
Absolute stereochemistry. Rotation (+).



RN 774232-23-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1α,3α,5α)-3,5-dihydroxycyclohexyl]-3-(2-fluoro-4-methoxyphenyl)-3,4-dihydro-7-[(4-methoxyphenyl)amino]-, rel- (9CI) (CA INDEX NAME)

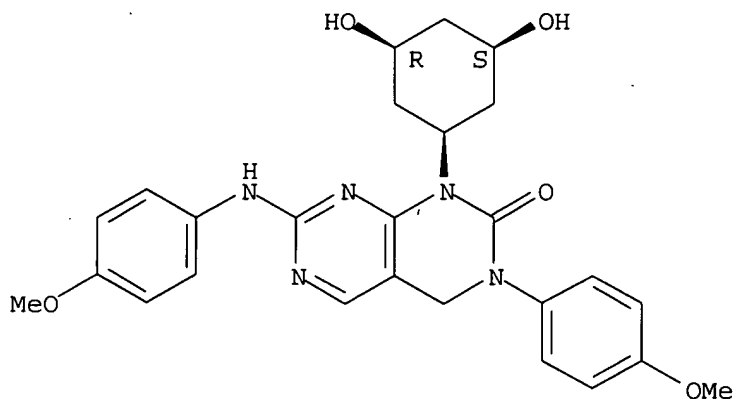
Relative stereochemistry.



RN 774232-24-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1 α ,3 α ,5 α)-3,5-dihydroxycyclohexyl]-3,4-dihydro-3-(4-methoxyphenyl)-7-[(4-methoxyphenyl)amino] - (9CI) (CA INDEX NAME)

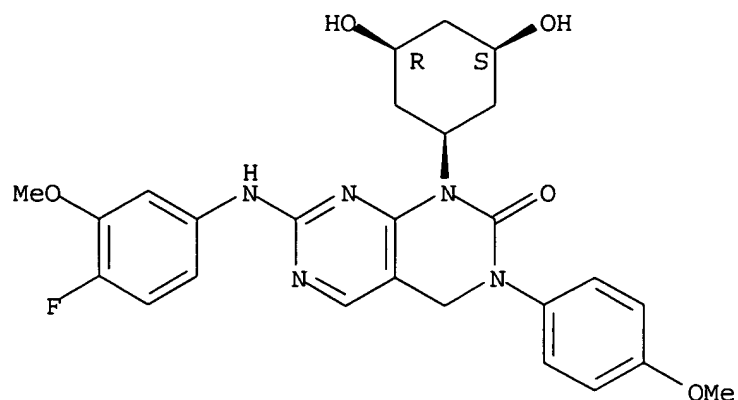
Relative stereochemistry.



RN 774232-25-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1 α ,3 α ,5 α)-3,5-dihydroxycyclohexyl]-7-[(4-fluoro-3-methoxyphenyl)amino]-3,4-dihydro-3-(4-methoxyphenyl) - (9CI) (CA INDEX NAME)

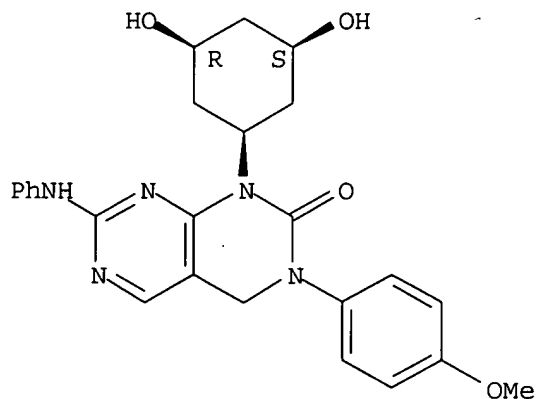
Relative stereochemistry.



RN 774232-26-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1 α ,3 α ,5 α)-3,5-dihydroxycyclohexyl]-3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino)-(9CI) (CA INDEX NAME)

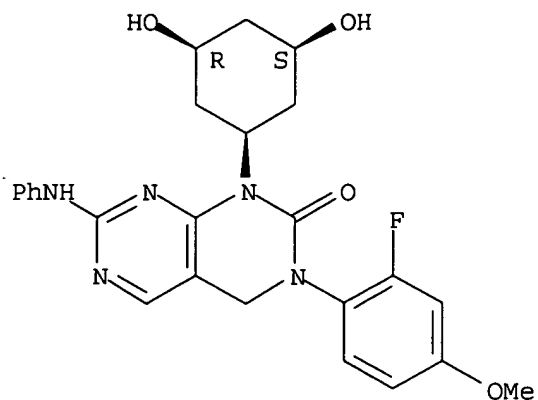
Relative stereochemistry.



RN 774232-27-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1 α ,3 α ,5 α)-3,5-dihydroxycyclohexyl]-3-(2-fluoro-4-methoxyphenyl)-3,4-dihydro-7-(phenylamino)-(9CI) (CA INDEX NAME)

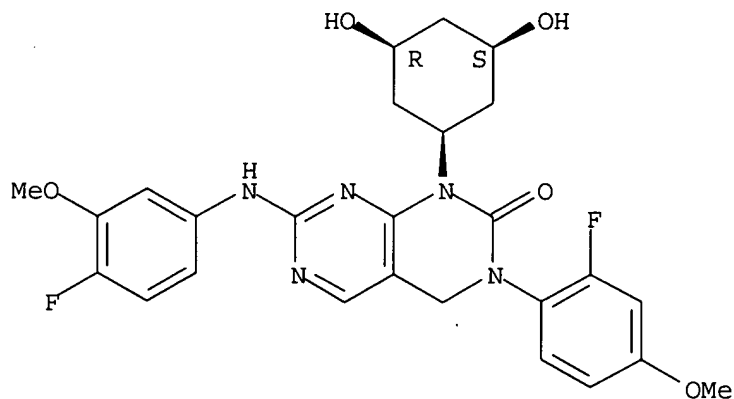
Relative stereochemistry.



RN 774232-28-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1 α ,3 α ,5 α)-3,5-dihydroxycyclohexyl]-3-(2-fluoro-4-methoxyphenyl)-7-[(4-fluoro-3-methoxyphenyl)amino]-3,4-dihydro- (9CI) (CA INDEX NAME)

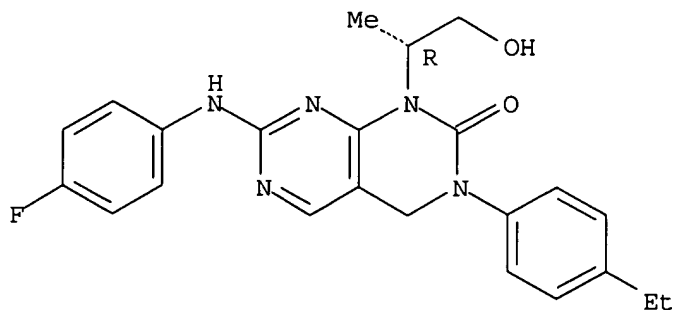
Relative stereochemistry.



RN 774232-29-0 HCAPLUS

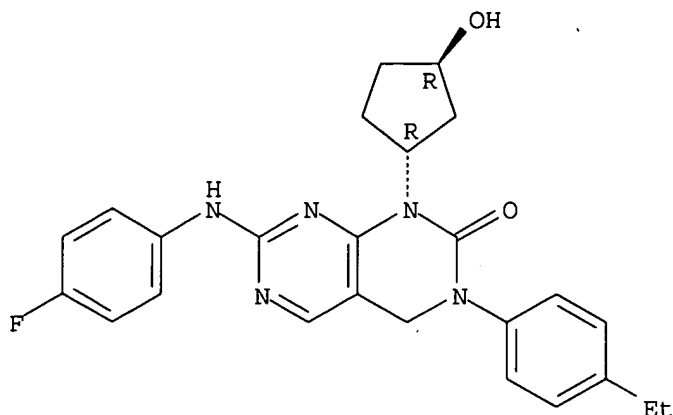
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-ethylphenyl)-7-[(4-fluorophenyl)amino]-3,4-dihydro-1-[(1R)-2-hydroxy-1-methylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

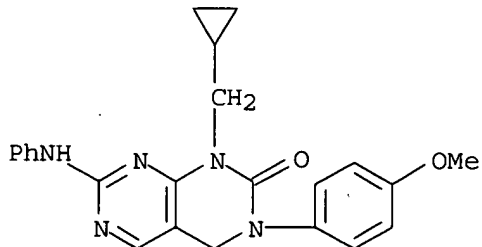


RN 774232-30-3 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(4-ethylphenyl)-7-[(4-fluorophenyl)amino]-3,4-dihydro-1-[(1R,3S)-3-hydroxycyclopentyl]-, rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.

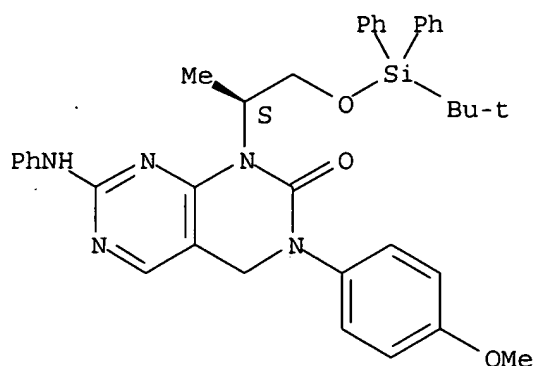


RN 774232-31-4 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-(cyclopropylmethyl)-3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino)- (9CI) (CA INDEX NAME)



IT 774232-74-5P 774232-75-6P 774232-78-9P
 774232-79-0P 774232-80-3P 774232-86-9P
 774232-90-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (intermediate; preparation of pyrimido[4,5-d]pyrimidinones as selective inhibitors of both KDR and FGFR kinases)
 RN 774232-74-5 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1S)-2-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]-1-methylethyl]-3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino)- (9CI) (CA INDEX NAME)

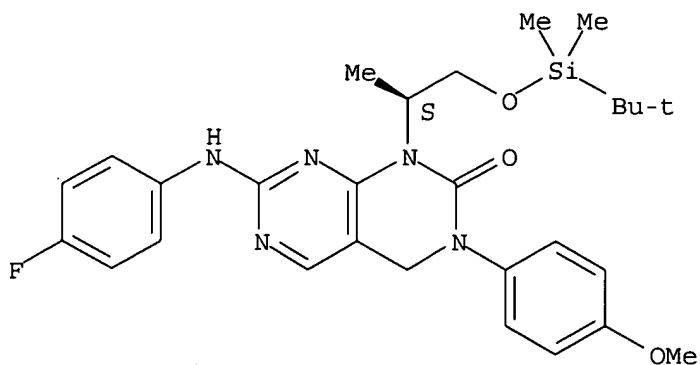
Absolute stereochemistry.



RN 774232-75-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1S)-2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-methylethyl]-7-[(4-fluorophenyl)amino]-3,4-dihydro-3-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

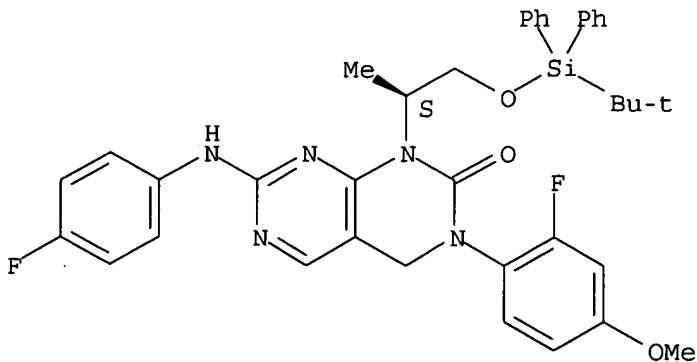
Absolute stereochemistry.



RN 774232-78-9 HCAPLUS

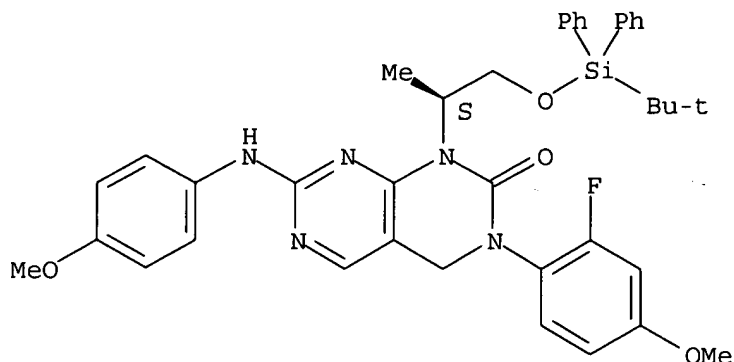
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1S)-2-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]-1-methylethyl]-7-[(4-fluorophenyl)amino]-3-(2-fluoro-4-methoxyphenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



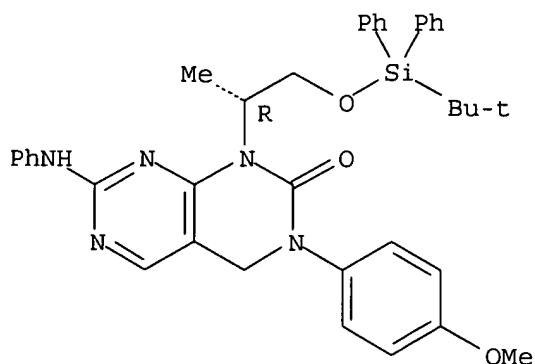
RN 774232-79-0 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1S)-2-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]-1-methylethyl]-3-(2-fluoro-4-methoxyphenyl)-3,4-dihydro-7-[(4-methoxyphenyl)amino] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



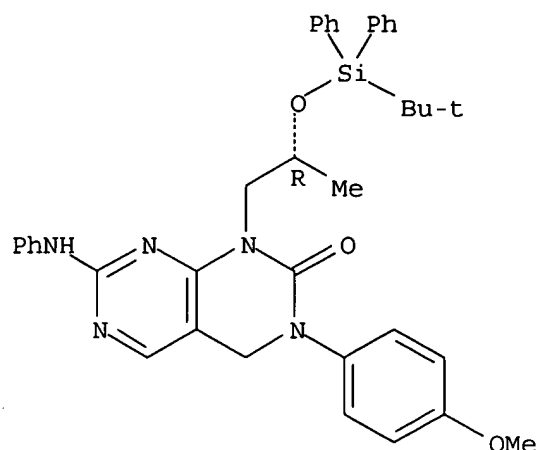
RN 774232-80-3 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1R)-2-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]-1-methylethyl]-3-(4-methoxyphenyl)-3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 774232-86-9 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(2R)-2-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]propyl]-3-(4-methoxyphenyl)-7-(phenylamino) - (9CI) (CA INDEX NAME)

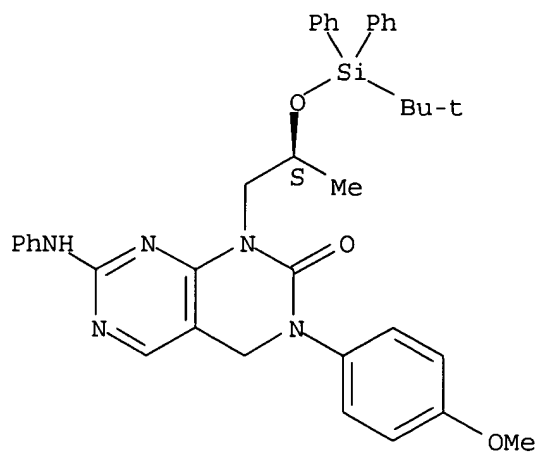
Absolute stereochemistry.



RN 774232-90-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(2S)-2-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]propyl]-3,4-dihydro-3-(4-methoxyphenyl)-7-(phenylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L27 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:412946 HCAPLUS

DOCUMENT NUMBER: 140:423694

TITLE: Preparation of pyrimidopyrimidinone derivatives having anticancer activity

INVENTOR(S): Dermatakis, Apostolos; Kabat, Marek Michal; Luk, Kin-Chun; Rossman, Pamela Loreen; So, Sung-Sau

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 85 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|-------------------|-----------------|------------|
| WO 2004041822 | A1 | 20040521 | WO 2003-EP11896 | 20031027 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004110773 | A1 | 20040610 | US 2003-689438 | 20031020 |
| US 2005075272 | A1 | 20050407 | US 2003-689235 | 20031020 |
| PRIORITY APPLN. INFO.: | | | US 2002-423670P | P 20021104 |
| OTHER SOURCE(S): | | MARPAT 140:423694 | | |
| GI | | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. I [R1 = H, (substituted)alkyl, (substituted)aryl, (substituted)heteroaryl, (substituted)heterocycle, (substituted)cycloalkyl, (substituted)alkenyl, (substituted)alkynyl; R2, R3, R4 = H, halo, COR10, CO2R10, CONR10R11, SOR10, SO2R10, CN, or NO2; R5, R6, R7, R8 = H, (substituted)alkyl, (substituted)amino, OH, halo, etc.; R9 = H, -COOCR12R13OCOR14, or COR15; R10, R11 = H, (substituted)alkyl, (substituted)cycloalkyl, (substituted)heterocycle, etc.; R12, R13 = H, alkyl; R14 = (substituted)alkyl; R15 = H, alkyl or cycloamines with 3-7 atoms] were prepared as anti-proliferative agents for the treatment or control of solid tumors, in particular breast, colon, lung and prostate tumors. For example, reaction of 7-chloro-3-(4-methoxyphenyl)-4-methyl-1-phenyl-3,4-dihydro-1H-pyrimido[4,5-d]-2-one (preparation given) with aniline yielded compound II. The latter showed inhibition of KDR, FGFR, EGFR and PDGFR with IC50 < 10 µM.

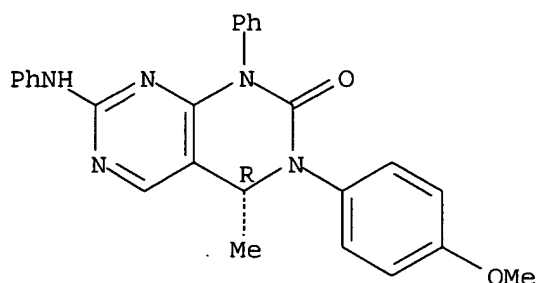
IT **690991-80-1P 690991-82-3P**

RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrimidopyrimidinone derivs. having anticancer activity)

RN 690991-80-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-3-(4-methoxyphenyl)-4-methyl-1-phenyl-7-(phenylamino)-, (4R)- (9CI) (CA INDEX NAME)

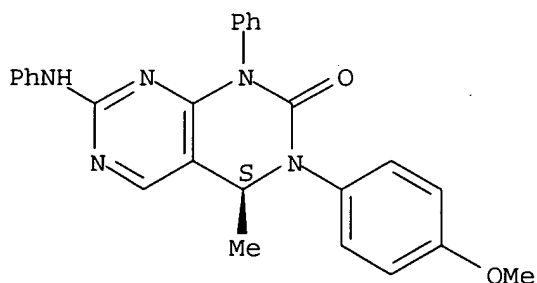
Absolute stereochemistry.



RN 690991-82-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-3-(4-methoxyphenyl)-4-methyl-1-phenyl-7-(phenylamino)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

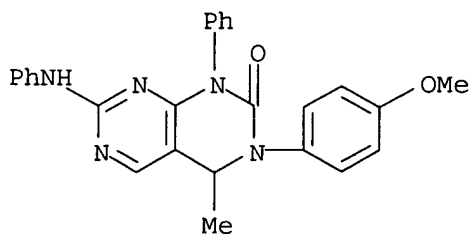


IT 690991-78-7P 690991-94-7P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyrimidopyrimidinone derivs. having anticancer activity)

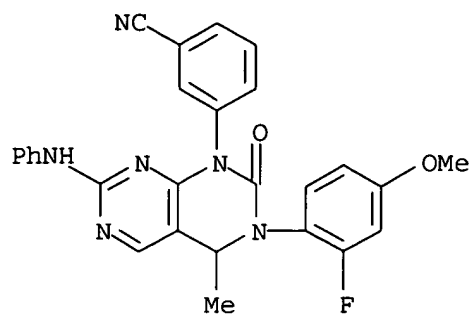
RN 690991-78-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-3-(4-methoxyphenyl)-4-methyl-1-phenyl-7-(phenylamino)- (9CI) (CA INDEX NAME)



RN 690991-94-7 HCAPLUS

CN Benzonitrile, 3-[3-(2-fluoro-4-methoxyphenyl)-3,4-dihydro-4-methyl-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]- (9CI) (CA INDEX NAME)



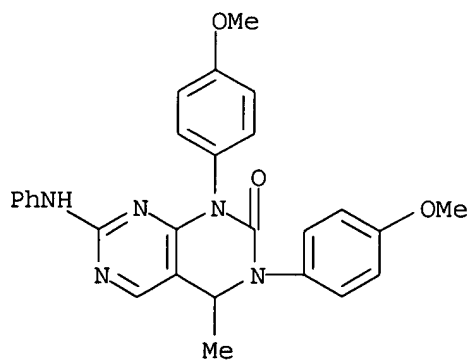
IT 690991-84-5P 690991-86-7P 690991-88-9P
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 690992-04-2P 690992-06-4P 690992-12-2P
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 690992-27-9P 690992-29-1P 690992-30-4P
 690992-32-6P 690992-34-8P 690992-36-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of pyrimidopyrimidinone derivs. having anticancer activity)

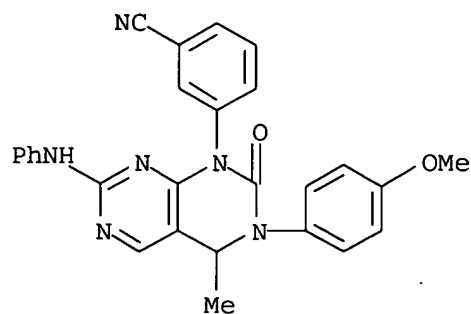
RN 690991-84-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1,3-bis(4-methoxyphenyl)-4-methyl-7-(phenylamino)- (9CI) (CA INDEX NAME)



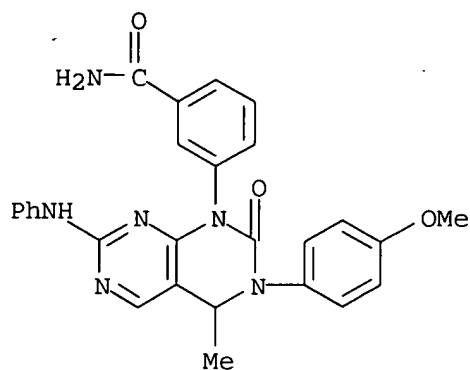
RN 690991-86-7 HCAPLUS

CN Benzonitrile, 3-[3,4-dihydro-3-(4-methoxyphenyl)-4-methyl-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]- (9CI) (CA INDEX NAME)



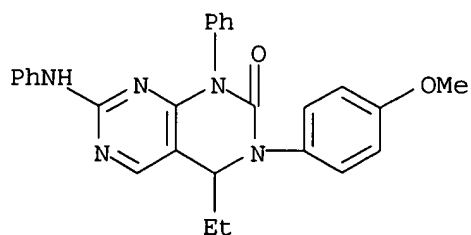
RN 690991-88-9 HCAPLUS

CN Benzamide, 3-[3,4-dihydro-3-(4-methoxyphenyl)-4-methyl-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]- (9CI) (CA INDEX NAME)



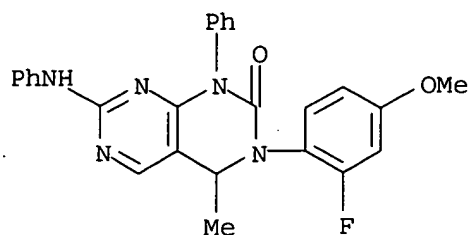
RN 690991-90-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 4-ethyl-3,4-dihydro-3-(4-methoxyphenyl)-1-phenyl-7-(phenylamino)- (9CI) (CA INDEX NAME)

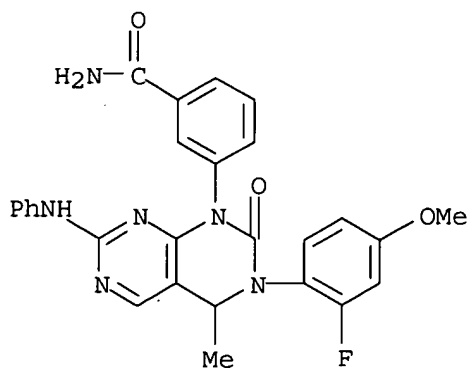


RN 690991-92-5 HCAPLUS

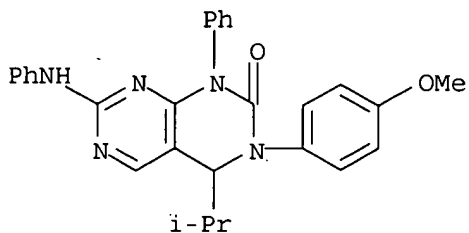
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-fluoro-4-methoxyphenyl)-3,4-dihydro-4-methyl-1-phenyl-7-(phenylamino)- (9CI) (CA INDEX NAME)



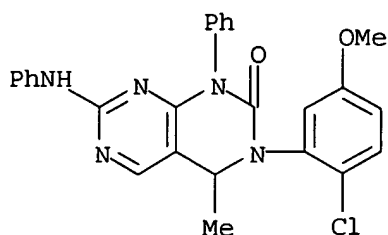
RN 690991-96-9 HCAPLUS
 CN Benzamide, 3-[3-(2-fluoro-4-methoxyphenyl)-3,4-dihydro-4-methyl-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]- (9CI) (CA INDEX NAME)



RN 690991-98-1 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(4-methoxyphenyl)-4-(1-methylethyl)-1-phenyl-7-(phenylamino)- (9CI) (CA INDEX NAME)



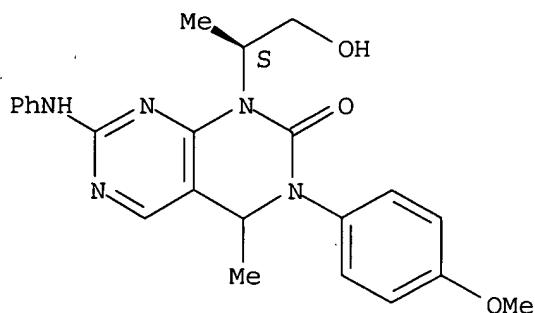
RN 690992-00-8 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chloro-5-methoxyphenyl)-3,4-dihydro-4-methyl-1-phenyl-7-(phenylamino)- (9CI) (CA INDEX NAME)



RN 690992-02-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-[(1S)-2-hydroxy-1-methylethyl]-3-(4-methoxyphenyl)-4-methyl-7-(phenylamino)- (9CI) (CA INDEX NAME)

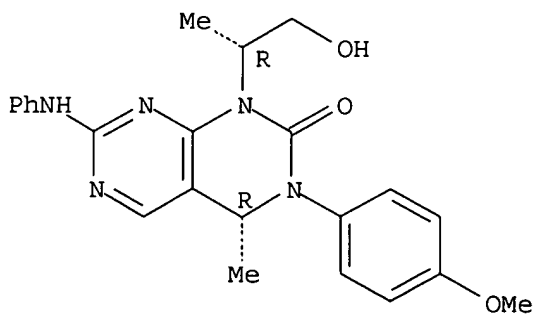
Absolute stereochemistry.



RN 690992-04-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-[(1R)-2-hydroxy-1-methylethyl]-3-(4-methoxyphenyl)-4-methyl-7-(phenylamino)-, (4R)- (9CI) (CA INDEX NAME)

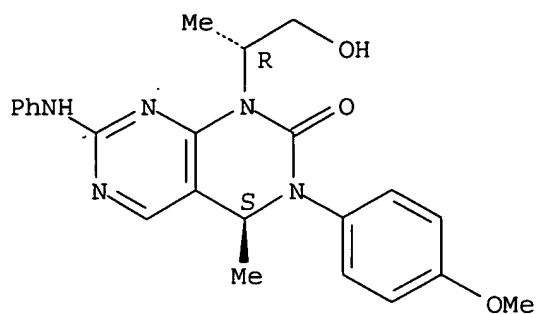
Absolute stereochemistry. Rotation (+).



RN 690992-06-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-[(1R)-2-hydroxy-1-methylethyl]-3-(4-methoxyphenyl)-4-methyl-7-(phenylamino)-, (4S)- (9CI) (CA INDEX NAME)

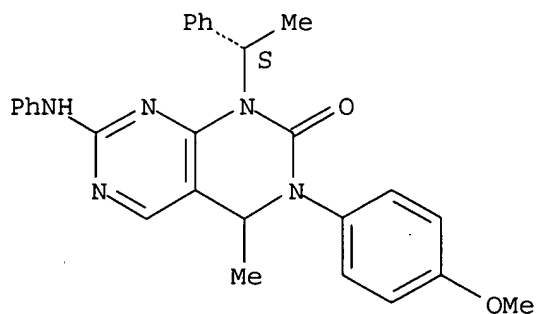
Absolute stereochemistry. Rotation (-).



RN 690992-12-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-3-(4-methoxyphenyl)-4-methyl-7-(phenylamino)-1-[(1S)-1-phenylethyl]- (9CI) (CA INDEX NAME)

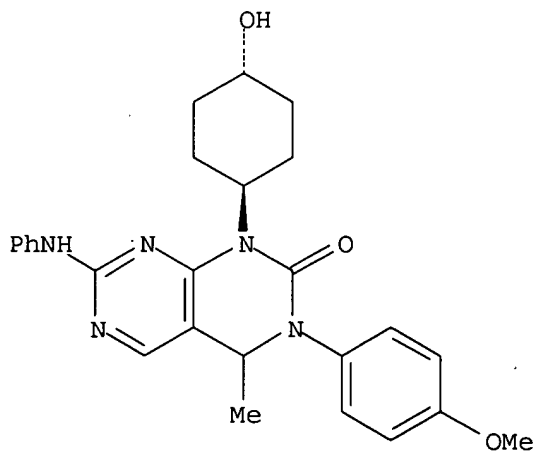
Absolute stereochemistry.



RN 690992-16-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-(trans-4-hydroxycyclohexyl)-3-(4-methoxyphenyl)-4-methyl-7-(phenylamino)- (9CI) (CA INDEX NAME)

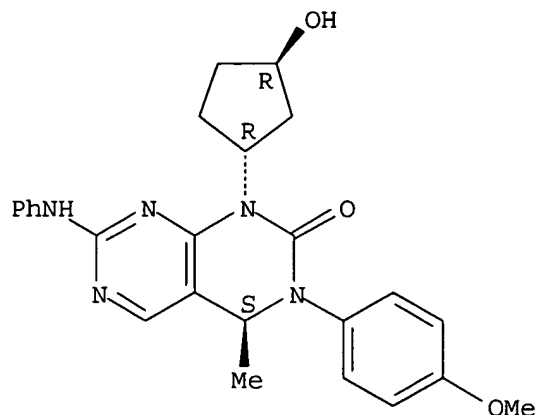
Relative stereochemistry.



RN 690992-17-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-[(1R,3R)-3-hydroxycyclopentyl]-3-(4-methoxyphenyl)-4-methyl-7-(phenylamino)-, (4S)-(9CI) (CA INDEX NAME)

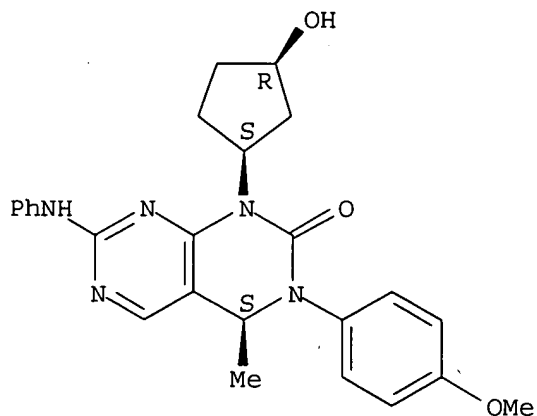
Absolute stereochemistry.



RN 690992-19-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-[(1S,3R)-3-hydroxycyclopentyl]-3-(4-methoxyphenyl)-4-methyl-7-(phenylamino)-, (4S)-(9CI) (CA INDEX NAME)

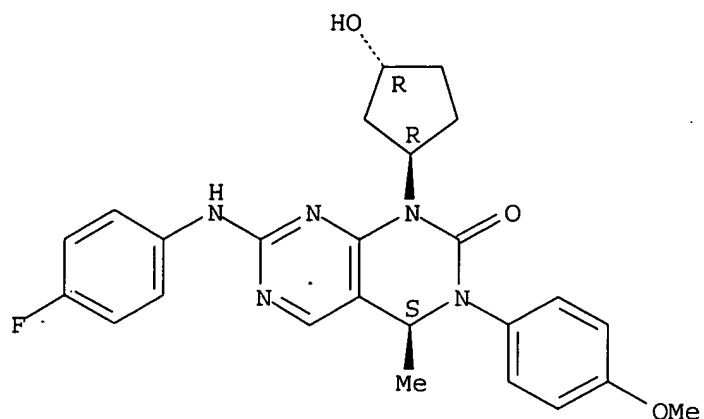
Absolute stereochemistry.



RN 690992-21-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(4-fluorophenyl)amino]-3,4-dihydro-1-[(1R,3R)-3-hydroxycyclopentyl]-3-(4-methoxyphenyl)-4-methyl-, (4S)-(9CI) (CA INDEX NAME)

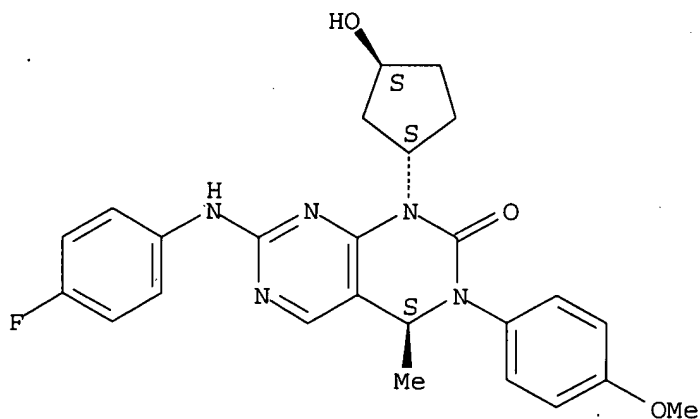
Absolute stereochemistry.



RN 690992-23-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(4-fluorophenyl)amino]-3,4-dihydro-1-[(1S,3S)-3-hydroxycyclopentyl]-3-(4-methoxyphenyl)-4-methyl-, (4S)-(9CI) (CA INDEX NAME)

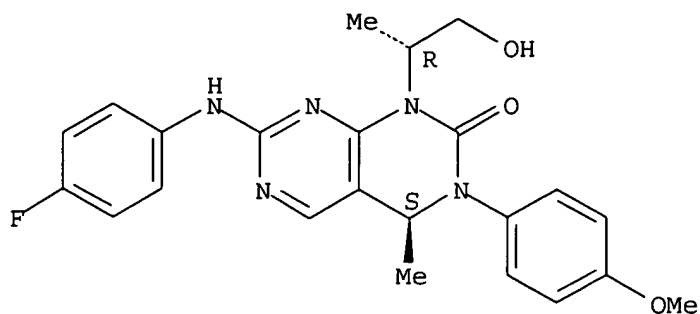
Absolute stereochemistry.



RN 690992-25-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(4-fluorophenyl)amino]-3,4-dihydro-1-[(1R)-2-hydroxy-1-methylethyl]-3-(4-methoxyphenyl)-4-methyl-, (4S)-(9CI) (CA INDEX NAME)

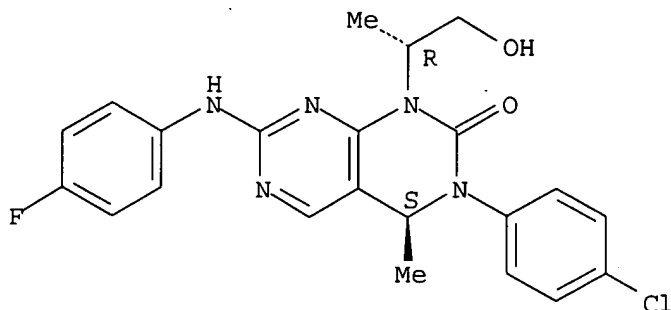
Absolute stereochemistry.



RN 690992-27-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(4-chlorophenyl)-7-[(4-fluorophenyl)amino]-3,4-dihydro-1-[(1R)-2-hydroxy-1-methylethyl]-4-methyl-, (4S)- (9CI) (CA INDEX NAME)

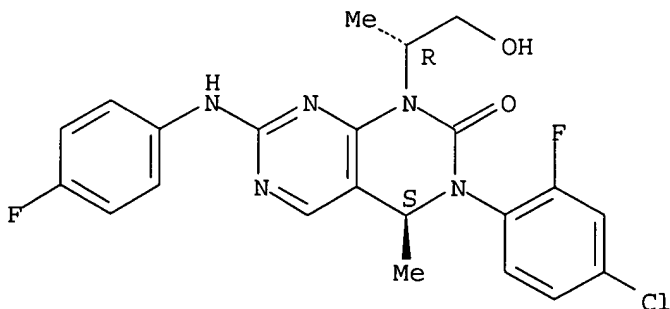
Absolute stereochemistry.



RN 690992-29-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(4-chloro-2-fluorophenyl)-7-[(4-fluorophenyl)amino]-3,4-dihydro-1-[(1R)-2-hydroxy-1-methylethyl]-4-methyl-, (4S)- (9CI) (CA INDEX NAME)

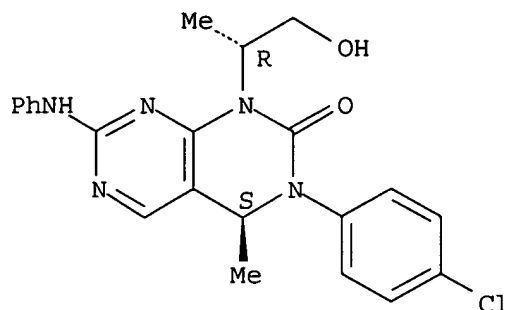
Absolute stereochemistry.



RN 690992-30-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(4-chlorophenyl)-3,4-dihydro-1-[(1R)-2-hydroxy-1-methylethyl]-4-methyl-7-(phenylamino)-, (4S)- (9CI) (CA INDEX NAME)

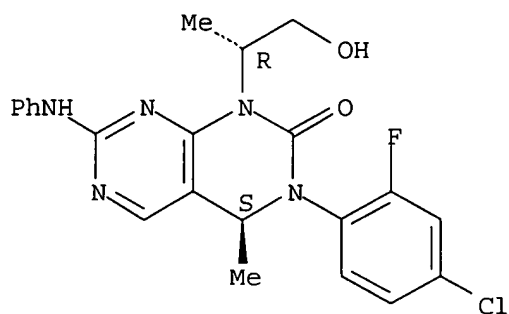
Absolute stereochemistry.



RN 690992-32-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(4-chloro-2-fluorophenyl)-3,4-dihydro-1-[(1R)-2-hydroxy-1-methylethyl]-4-methyl-7-(phenylamino)-, (4S)-(9CI) (CA INDEX NAME)

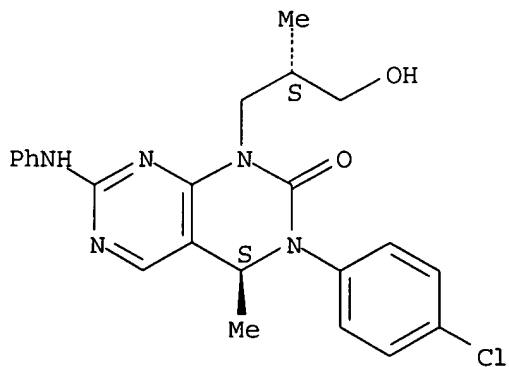
Absolute stereochemistry.



RN 690992-34-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(4-chlorophenyl)-3,4-dihydro-1-[(2S)-3-hydroxy-2-methylpropyl]-4-methyl-7-(phenylamino)-, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

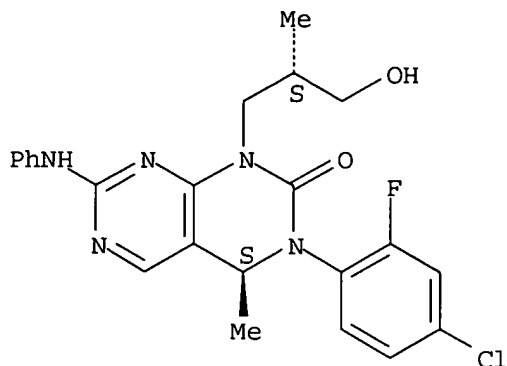


RN 690992-36-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(4-chloro-2-fluorophenyl)-3,4-

dihydro-1-[(2S)-3-hydroxy-2-methylpropyl]-4-methyl-7-(phenylamino)-, (4S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 690992-65-5P 690992-70-2P 690992-72-4P

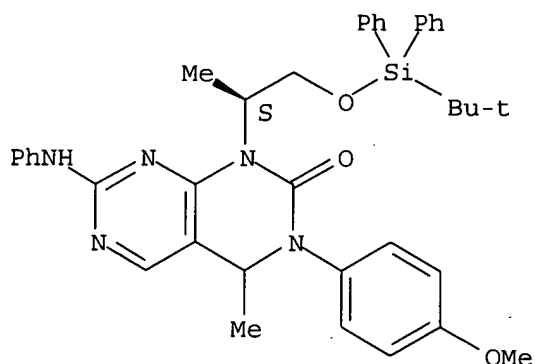
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation of pyrimidopyrimidinone derivs. having anticancer activity)

RN 690992-65-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1S)-2-[[[1,1-dimethylethyl]diphenylsilyl]oxy]-1-methylethyl]-3,4-dihydro-3-(4-methoxyphenyl)-4-methyl-7-(phenylamino)- (9CI) (CA INDEX NAME)

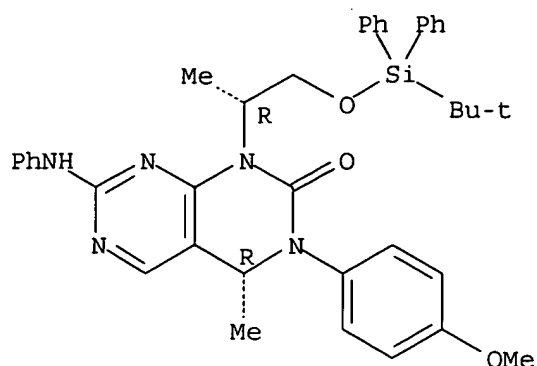
Absolute stereochemistry.



RN 690992-70-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1R)-2-[[[1,1-dimethylethyl]diphenylsilyl]oxy]-1-methylethyl]-3,4-dihydro-3-(4-methoxyphenyl)-4-methyl-7-(phenylamino)-, (4R)- (9CI) (CA INDEX NAME)

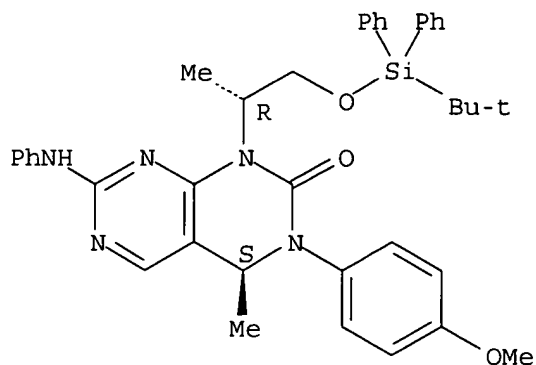
Absolute stereochemistry.



RN 690992-72-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[(1R)-2-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]-1-methylethyl]-3,4-dihydro-3-(4-methoxyphenyl)-4-methyl-7-(phenylamino)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:412945 HCAPLUS

DOCUMENT NUMBER: 140:423693

TITLE: Preparation of pyrimido Src tyrosine kinase inhibitors as anti-proliferative agents for the treatment of cancer

INVENTOR(S): Luk, Kin-Chun; Rossmann, Pamela Loreen; Scheiblich, Stefan; So, Sung-Sau

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|-------|-----------------|-------|
| ----- | ---- | ----- | ----- | ----- |

WO 2004041821 A1 20040521 WO 2003-EP311892 20031027
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 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
 GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
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 PRIORITY APPLN. INFO.: US 2002-423670P P 20021104
 OTHER SOURCE(S): MARPAT 140:423693
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

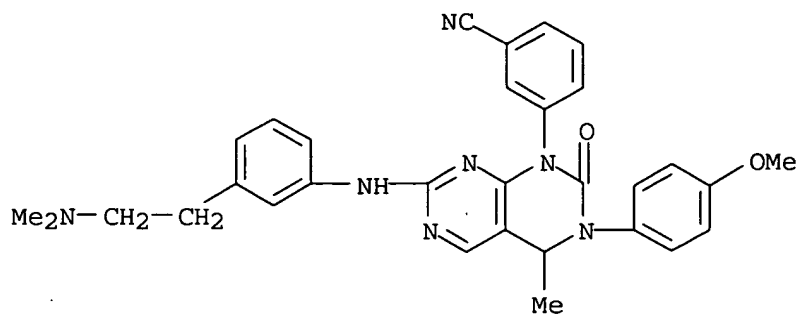
AB MovPyrimido compds. I (R1 = H, alkyl, substituted alkyl, aryl, heteroaryl, heterocycle, cycloalkyl, alkenyl, alkynyl; R2,R3,R4 independently = H, amine, alkoxy, sulfanyl, alkyl, cycloalkyl, alkenyl, alkynyl; R5, R6, R7, R8 independently = H, lower alkyl, amine, OH, alkoxy, sulfanyl, halogen, ketone, ester, amide, sulfonyl, CN; R9 = H, diester, ketone), that are selective inhibitors of the Src family of tyrosine kinases are prepared for the treatment of breast, colon, pancreatic, and hepatic cancers. Thus, 1-(2,4-dichloro-pyrimidin-5-yl)-ethanol was treated with phosphorus oxybromide and diisopropyl amine to give 2,4-dichloro-5-(1-bromoethyl)-pyrimidine which was treated with p-anisidine, potassium carbonate, and potassium iodide to give the corresponding amine. The above amine was reacted with 3-cyanophenyl isocyanate in toluene to give II. II was reacted with acetic acid 2-(3-amino-phenyl)-Et ester, followed by treatment with potassium carbonate in methanol to give III. III showed and IC50 of less than 1.0 μ M against Src tyrosine kinase. Also disclosed are pharmaceutical compns. containing these compds. and the use for treating cancer.

IT 690995-25-6P 690995-29-0P 690995-31-4P
 690995-33-6P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (preparation of pyrimido Src tyrosine kinase inhibitors as anti-proliferative agents for the treatment of cancer)

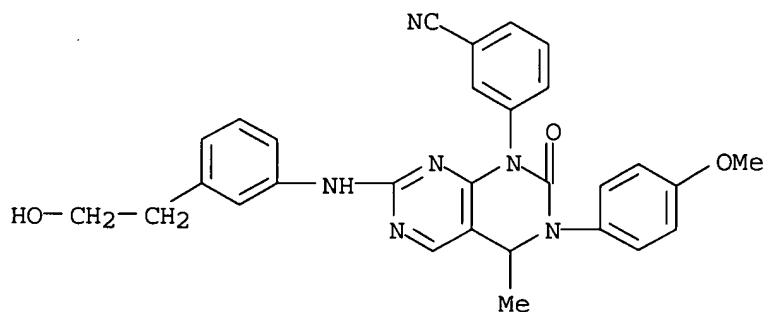
RN 690995-25-6 HCAPLUS

CN Benzonitrile, 3-[7-[[3-[2-(dimethylamino)ethyl]phenyl]amino]-3,4-dihydro-3-(4-methoxyphenyl)-4-methyl-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]- (9CI)
 (CA INDEX NAME)



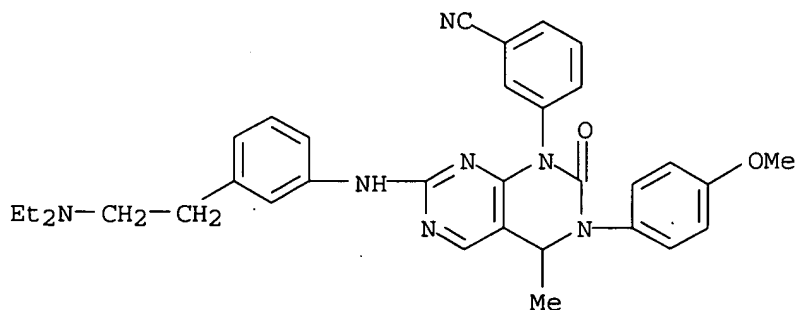
RN 690995-29-0 HCAPLUS

CN Benzonitrile, 3-[3,4-dihydro-7-[[3-[2-hydroxyethyl]phenyl]amino]-3-(4-methoxyphenyl)-4-methyl-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]- (9CI)
(CA INDEX NAME)



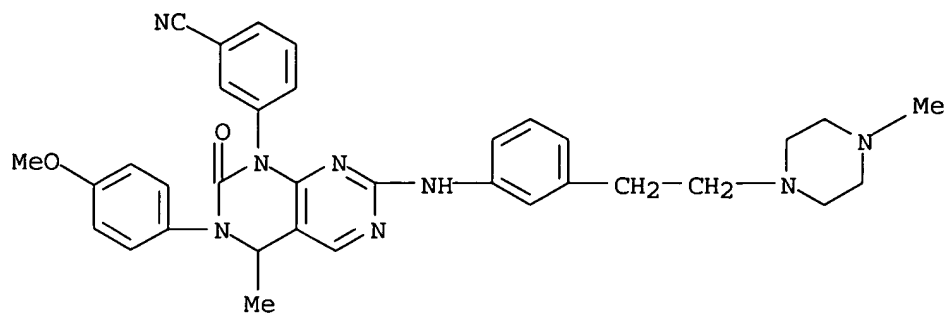
RN 690995-31-4 HCAPLUS

CN Benzonitrile, 3-[7-[[3-[2-(diethylamino)ethyl]phenyl]amino]-3,4-dihydro-3-(4-methoxyphenyl)-4-methyl-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]- (9CI)
(CA INDEX NAME)



RN 690995-33-6 HCAPLUS

CN Benzonitrile, 3-[3,4-dihydro-3-(4-methoxyphenyl)-4-methyl-7-[[3-[2-(4-methyl-1-piperazinyl)ethyl]phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]- (9CI) (CA INDEX NAME)



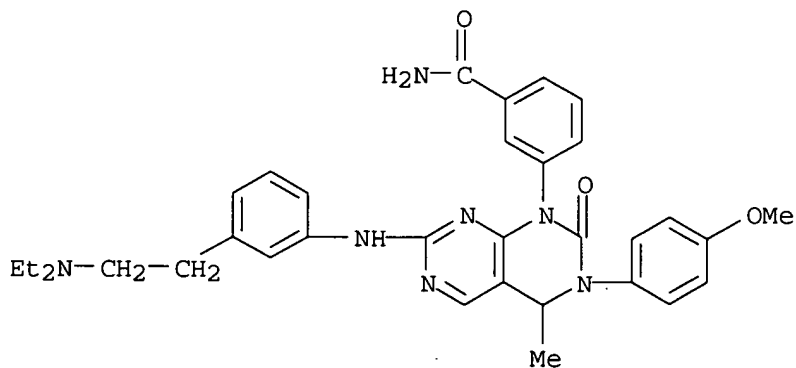
IT 690995-35-8P 690995-36-9P 690995-37-0P
690995-38-1P 690995-39-2P 690995-40-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrimido Src tyrosine kinase inhibitors as anti-proliferative agents for the treatment of cancer)

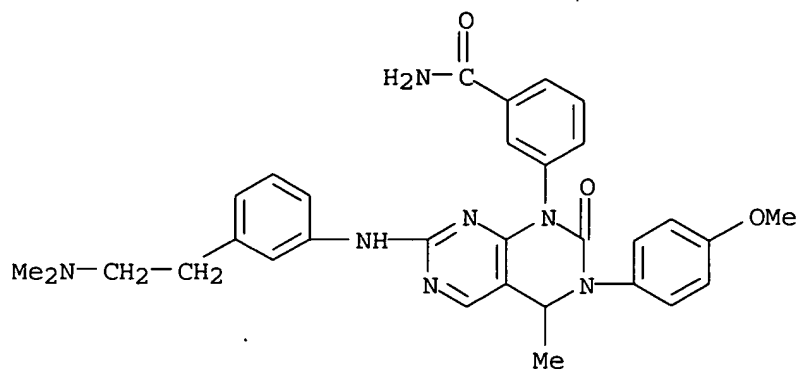
RN 690995-35-8 HCAPLUS

CN Benzamide, 3-[7-[[3-[2-(diethylamino)ethyl]phenyl]amino]-3,4-dihydro-3-(4-methoxyphenyl)-4-methyl-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]- (9CI)
(CA INDEX NAME)



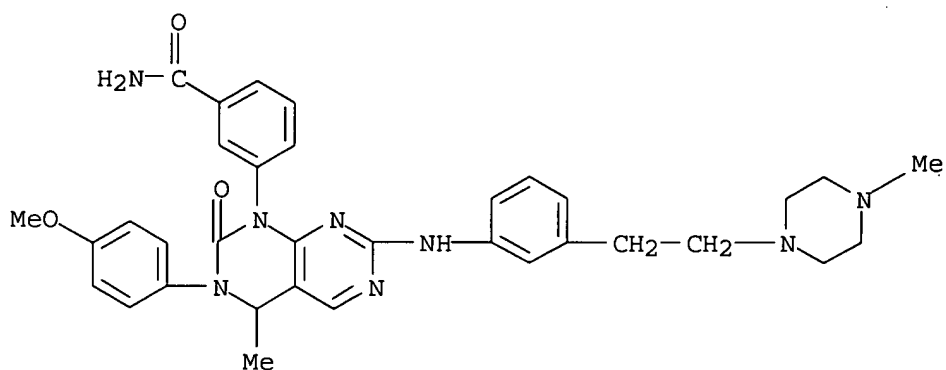
RN 690995-36-9 HCAPLUS

CN Benzamide, 3-[7-[[3-[2-(dimethylamino)ethyl]phenyl]amino]-3,4-dihydro-3-(4-methoxyphenyl)-4-methyl-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]- (9CI)
(CA INDEX NAME)



RN 690995-37-0 HCAPLUS

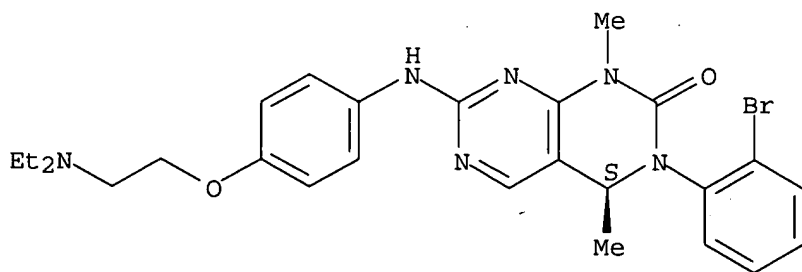
CN Benzamide, 3-[3,4-dihydro-3-(4-methoxyphenyl)-4-methyl-7-[[3-[2-(4-methyl-1-piperazinyl)ethyl]phenyl]amino]-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]-(9CI) (CA INDEX NAME)



RN 690995-38-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

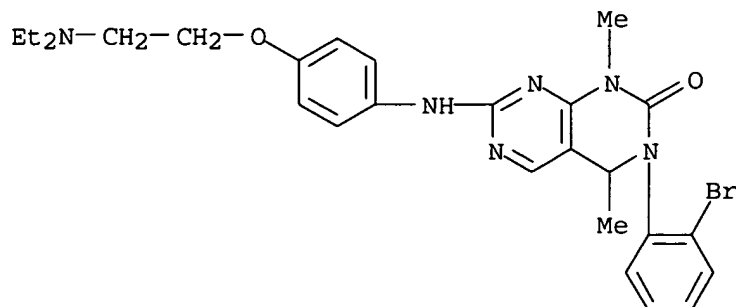
Absolute stereochemistry.



RN 690995-39-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1,4-dimethyl- (9CI) (CA INDEX NAME)

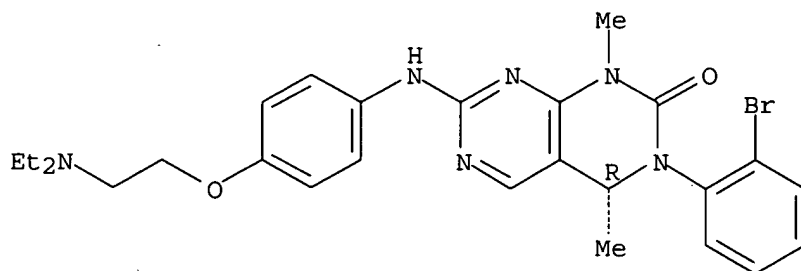
INDEX NAME)



RN 690995-40-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1,4-dimethyl-, (4R)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



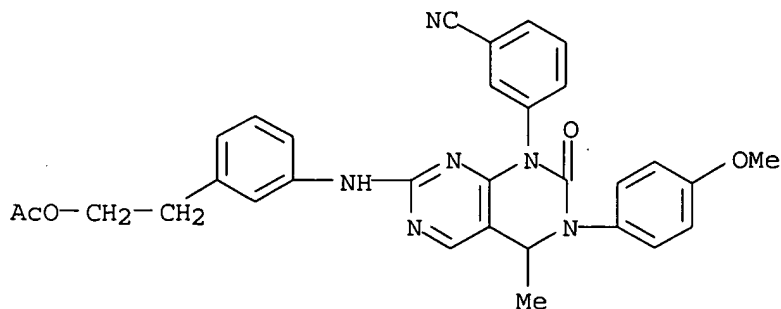
IT 690995-23-4P 690995-24-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyrimido Src tyrosine kinase inhibitors as anti-proliferative agents for the treatment of cancer)

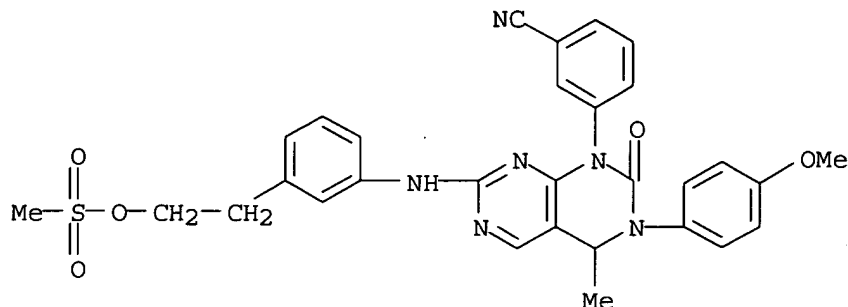
RN 690995-23-4 HCAPLUS

CN Benzonitrile, 3-[7-[[3-[2-(acetyloxy)ethyl]phenyl]amino]-3,4-dihydro-3-(4-methoxyphenyl)-4-methyl-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]- (9CI)
(CA INDEX NAME)



RN 690995-24-5 HCAPLUS

CN Benzonitrile, 3-[3,4-dihydro-3-(4-methoxyphenyl)-4-methyl-7-[[3-[2-
[(methylsulfonyl)oxy]ethyl]phenyl]amino]-2-oxypyrimido[4,5-d]pyrimidin-
1(2H)-yl]- (9CI) (CA INDEX NAME)



L27 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:372873 HCAPLUS

DOCUMENT NUMBER: 140:391294

TITLE: Preparation of amino-substituted dihydropyrimido[4,5-d]pyrimidinone derivatives as inhibitors of src family tyrosine kinases

INVENTOR(S): Cai, Jianping; Dimoudis, Nikolaos; Honold, Konrad; Luk, Kin-Chun; Scheiblich, Stefan; Sudergat, Hilke; Tiefenthaler, Georg; Tonn, Oliver

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 31 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

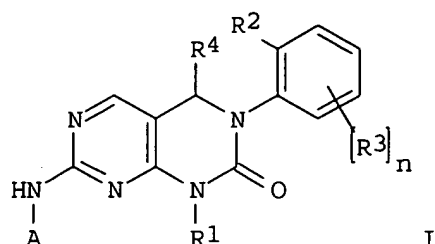
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 2004087600 | A1 | 20040506 | US 2003-697543 | 20031030 |
| WO 2004041823 | A1 | 20040521 | WO 2003-EP12203 | 20031103 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: EP 2002-24573 A 20021104

OTHER SOURCE(S): CASREACT 140:391294; MARPAT 140:391294

GI



I

AB The title compds. [I; R1 = H, alkyl, aryl, etc.; R2 = halo, CN, CF3; R3 = halo, OH, CN, etc.; n = 0-2; R4 = H, alkyl, alkoxy, CN; A = (un)substituted 2,3-dihydrobenzo[1,4]dioxin-6-yl, benzodioxane-6-yl, 3-oxo-3,4-dihydro-2H-benzo[1,4]thiazin-7-yl, etc.] which are protein kinase inhibitors, in particular they inhibit the src family tyrosine kinases, and therefore useful for the treatment of diseases mediated by src tyrosine kinases, including cell proliferative disorders such as cancer, were prepared. Thus, reacting 3-(2-bromophenyl)-3,4-dihydro-7-methanesulfonyl-1-methylpyrimido[4,5-d]pyrimidin-2(1H)-one with 2-hydroxymethyl-6-amino-1,4-benzodioxane (preparation given) afforded 3-(2-bromophenyl)-7-(2-hydroxymethyl-2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-1-methyl-3,4-dihydro-1H-pyrimido[4,5-d]pyrimidin-2(1H)-one which showed IC50 of 7.5 nM against src kinase, and IC50 of 6.3 nM against lck kinase. The pharmaceutical composition containing the compound I is claimed.

IT 686756-87-6P 686756-91-2P 686756-98-9P

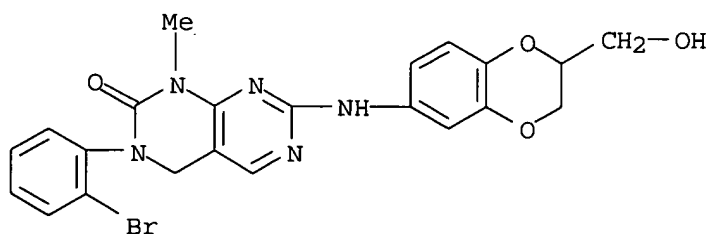
686757-21-1P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of amino-substituted dihydropyrimido[4,5-d]pyrimidinones as inhibitors of src family tyrosine kinases)

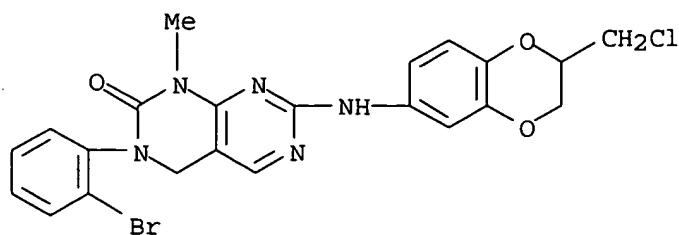
RN 686756-87-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[[2,3-dihydro-2-(hydroxymethyl)-1,4-benzodioxin-6-yl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



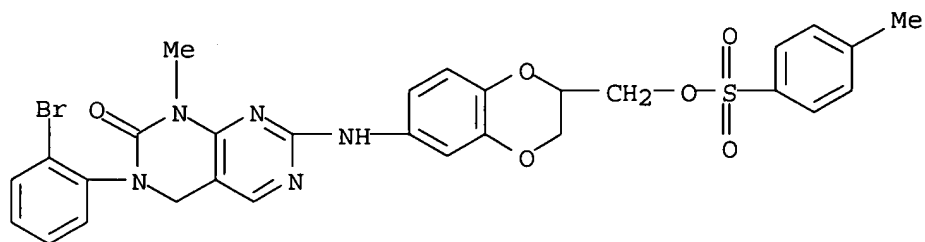
RN 686756-91-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[[2-(chloromethyl)-2,3-dihydro-1,4-benzodioxin-6-yl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



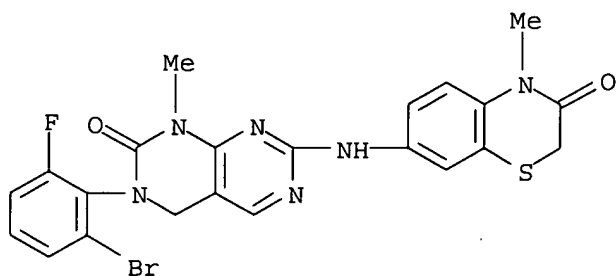
RN 686756-98-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[[[2,3-dihydro-2-[[[(4-methylphenyl)sulfonyl]oxy]methyl]-1,4-benzodioxin-6-yl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 686757-21-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromo-6-fluorophenyl)-7-[(3,4-dihydro-4-methyl-3-oxo-2H-1,4-benzothiazin-7-yl)amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



IT 686756-95-6P 686757-02-8P 686757-06-2P
 686757-10-8P 686757-14-2P 686757-17-5P
 686757-25-5P 686757-29-9P 686757-33-5P
 686757-37-9P 686757-40-4P 686757-44-8P
 686757-48-2P 686757-55-1P 686757-60-8P
 686757-65-3P 686757-70-0P 686757-73-3P
 686757-78-8P 686757-82-4P 686757-88-0P
 686757-93-7P 686759-58-0P 686759-62-6P
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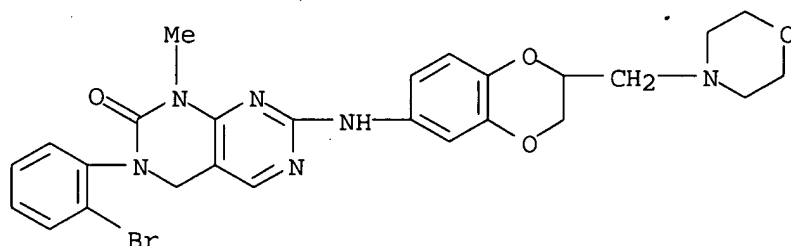
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 686761-25-1P 686761-29-5P 686761-36-4P
 686766-23-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of amino-substituted dihydropyrimido[4,5-d]pyrimidinones as
 inhibitors of src family tyrosine kinases)

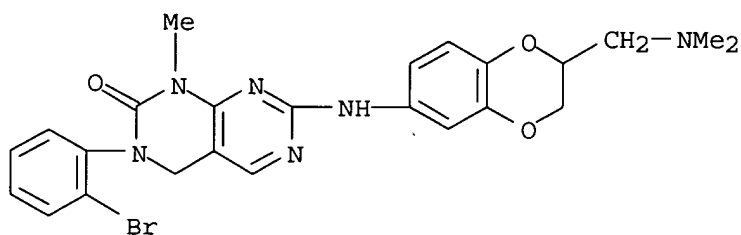
RN 686756-95-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[[2,3-dihydro-2-(4-morpholinylmethyl)-1,4-benzodioxin-6-yl]amino]-3,4-dihydro-1-methyl- (9CI)
 (CA INDEX NAME)



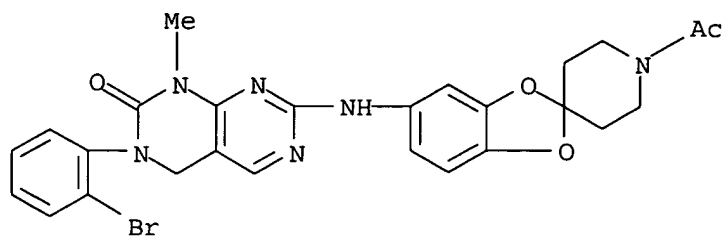
RN 686757-02-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[[2-
 [(dimethylamino)methyl]-2,3-dihydro-1,4-benzodioxin-6-yl]amino]-3,4-
 dihydro-1-methyl- (9CI) (CA INDEX NAME)



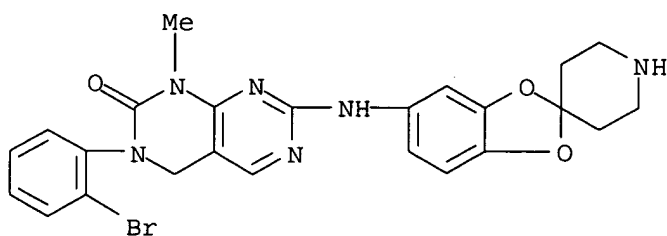
RN 686757-06-2 HCAPLUS

CN Spiro[1,3-benzodioxole-2,4'-piperidine], 1'-acetyl-5-[[6-(2-bromophenyl)-
 5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-
 (9CI) (CA INDEX NAME)



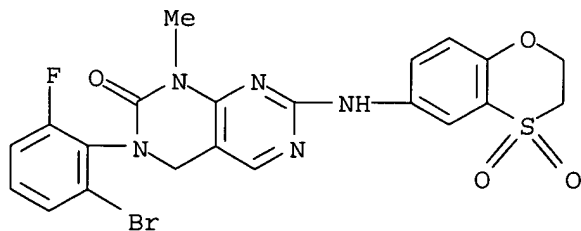
RN 686757-10-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-3,4-dihydro-1-methyl-7-((2,3-dihydro-4,4-dioxo-1,4-benzoxathiin-6-yl)amino)- (9CI) (CA INDEX NAME)



RN 686757-14-2 HCAPLUS

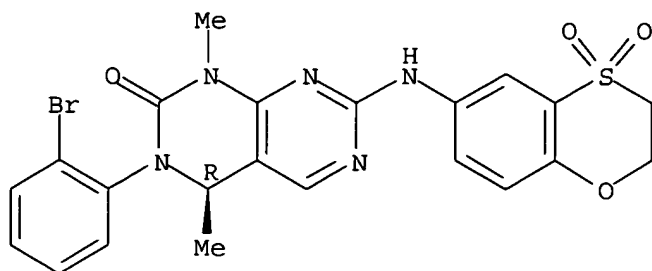
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromo-6-fluorophenyl)-7-[(2,3-dihydro-4,4-dioxo-1,4-benzoxathiin-6-yl)amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 686757-17-5 HCAPLUS

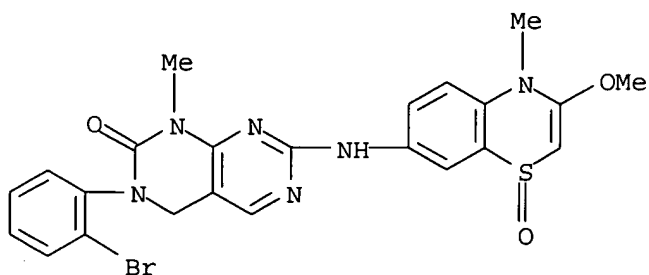
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[(2,3-dihydro-4,4-dioxo-1,4-benzoxathiin-6-yl)amino]-3,4-dihydro-1,4-dimethyl-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



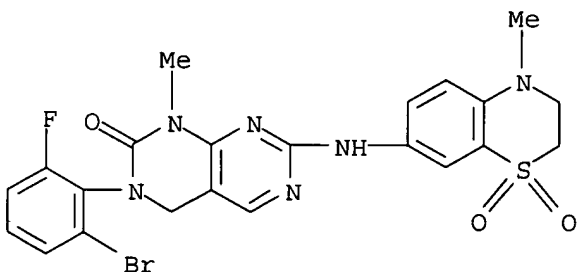
RN 686757-25-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-3,4-dihydro-7-[(3-methoxy-4-methyl-1-oxido-4H-1,4-benzothiazin-7-yl)amino]-1-methyl- (9CI) (CA INDEX NAME)



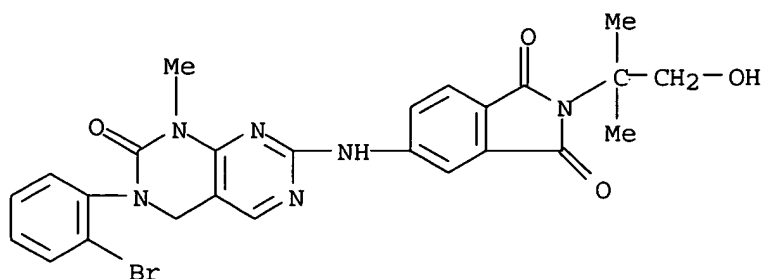
RN 686757-29-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromo-6-fluorophenyl)-7-[(3,4-dihydro-4-methyl-1,1-dioxido-2H-1,4-benzothiazin-7-yl)amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 686757-33-5 HCAPLUS

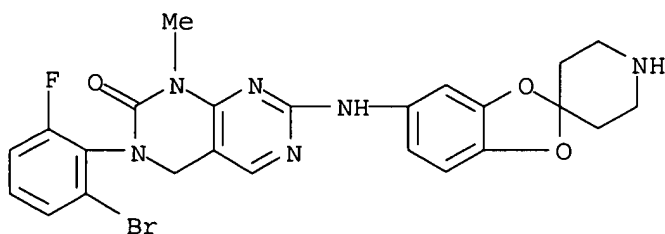
CN 1H-Isoindole-1,3(2H)-dione, 5-[[[6-(2-bromophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-2-(2-hydroxy-1,1-dimethylethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

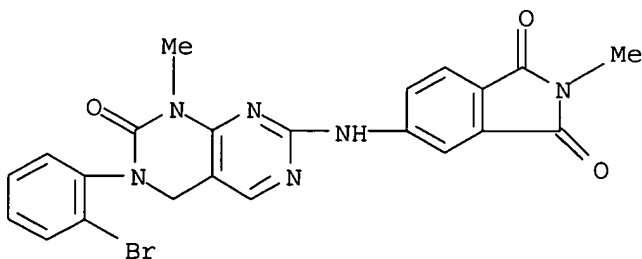
RN 686757-37-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromo-6-fluorophenyl)-3,4-dihydro-1-methyl-7-((spiro[1,3-benzodioxole-2,4'-piperidin]-5-ylamino))- (9CI) (CA INDEX NAME)



RN 686757-40-4 HCAPLUS

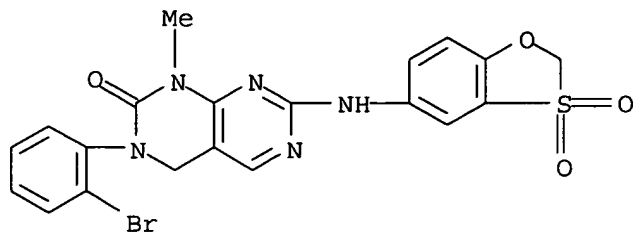
CN 1H-Isoindole-1,3(2H)-dione, 5-[[6-(2-bromophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

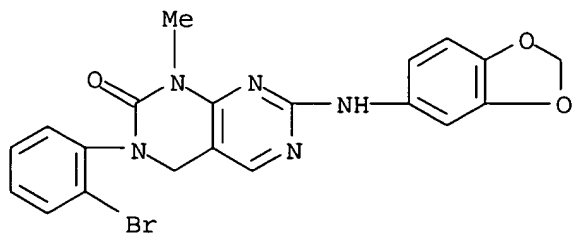
RN 686757-44-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[(3,3-dioxido-1,3-benzoxathiol-5-yl)amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



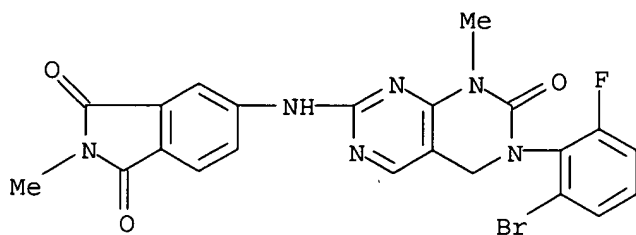
RN 686757-48-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-(1,3-benzodioxol-5-ylamino)-3-(2-bromophenyl)-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



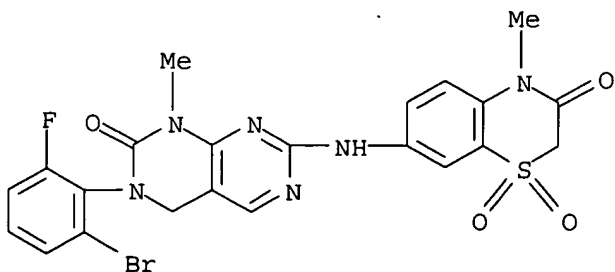
RN 686757-55-1 HCAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 5-[[6-(2-bromo-6-fluorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-2-methyl- (9CI) (CA INDEX NAME)



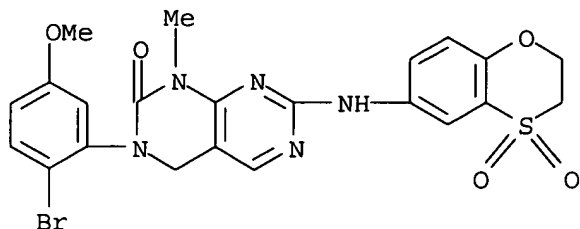
RN 686757-60-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromo-6-fluorophenyl)-7-[(3,4-dihydro-4-methyl-1,1-dioxido-3-oxo-2H-1,4-benzothiazin-7-yl)amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



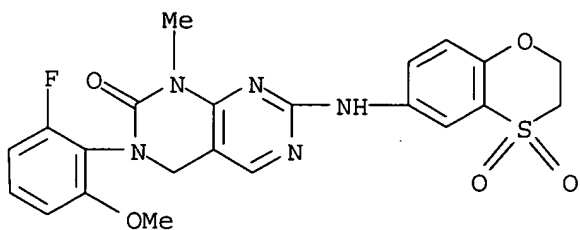
RN 686757-65-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromo-5-methoxyphenyl)-7-[(2,3-dihydro-4,4-dioxido-1,4-benzoxathiin-6-yl)amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 686757-70-0 HCAPLUS

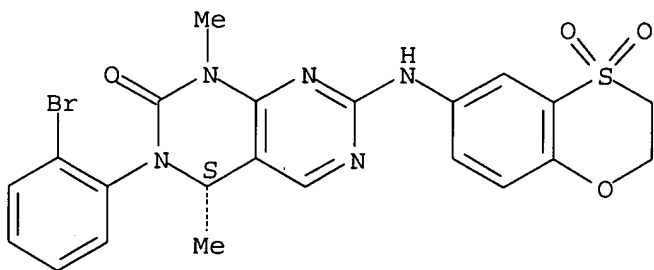
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(2,3-dihydro-4,4-dioxido-1,4-benzoxathiin-6-yl)amino]-3-(2-fluoro-6-methoxyphenyl)-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 686757-73-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[(2,3-dihydro-4,4-dioxido-1,4-benzoxathiin-6-yl)amino]-3,4-dihydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

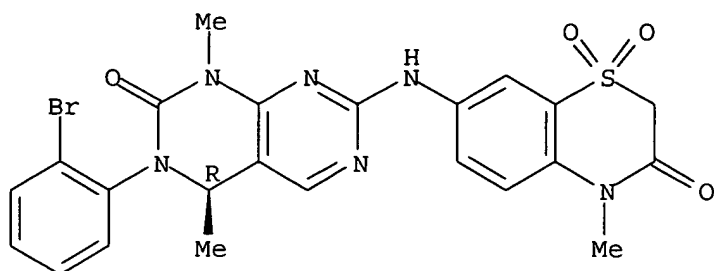
Absolute stereochemistry.



RN 686757-78-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[(3,4-dihydro-4-methyl-1,1-dioxido-3-oxo-2H-1,4-benzothiazin-7-yl)amino]-3,4-dihydro-1,4-dimethyl-, (4R)- (9CI) (CA INDEX NAME)

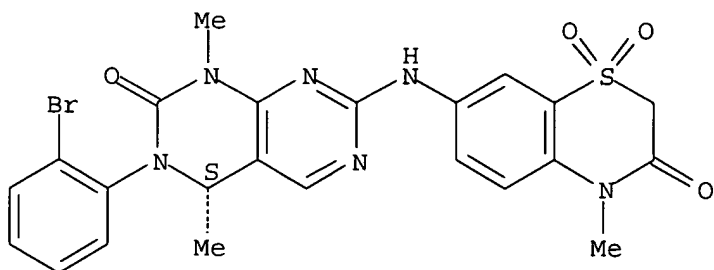
Absolute stereochemistry.



RN 686757-82-4 HCAPLUS

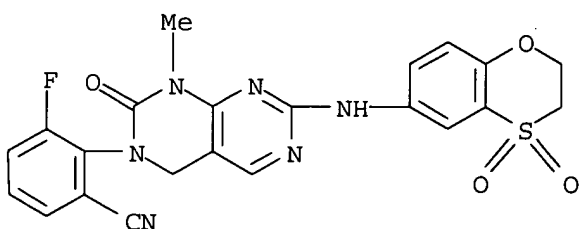
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[(3,4-dihydro-4-methyl-1,1-dioxido-3-oxo-2H-1,4-benzothiazin-7-yl)amino]-3,4-dihydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



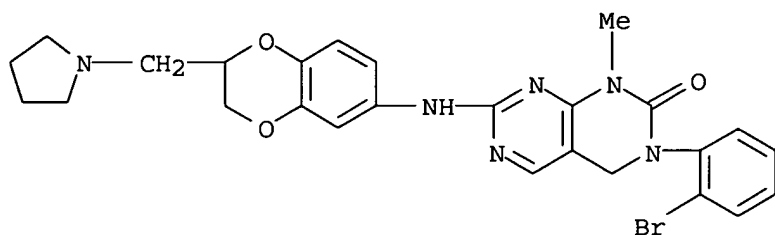
RN 686757-88-0 HCAPLUS

CN Benzonitrile, 2-[7-[(2,3-dihydro-4,4-dioxido-1,4-benzoxathiin-6-yl)amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]-3-fluoro- (9CI) (CA INDEX NAME)



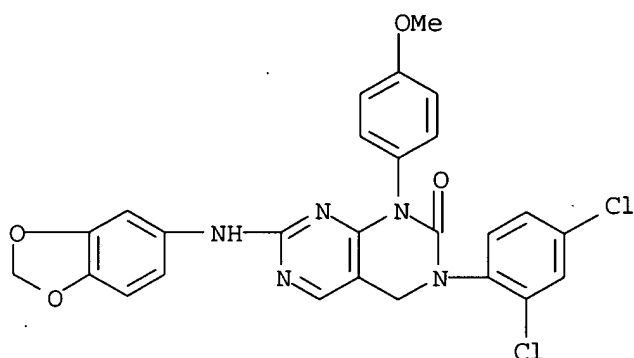
RN 686757-93-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[[2,3-dihydro-2-(1-pyrrolidinylmethyl)-1,4-benzodioxin-6-yl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



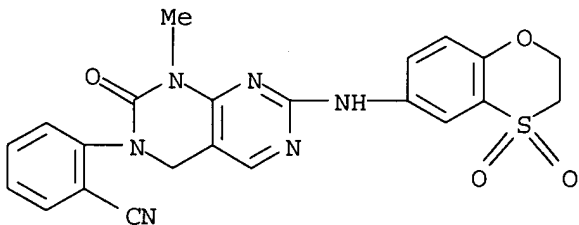
RN 686759-58-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-(1,3-benzodioxol-5-ylamino)-3-(2,4-dichlorophenyl)-3,4-dihydro-1-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



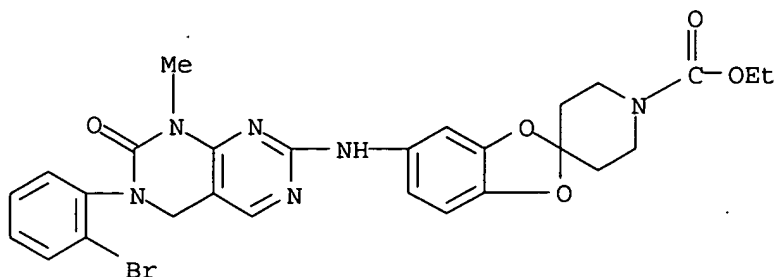
RN 686759-62-6 HCAPLUS

CN Benzonitrile, 2-[7-[(2,3-dihydro-4,4-dioxido-1,4-benzoxathiin-6-yl)amino]-1,4-dihydro-1-methyl-2-oxopyrimido[4,5-d]pyrimidin-3(2H)-yl]- (9CI) (CA INDEX NAME)



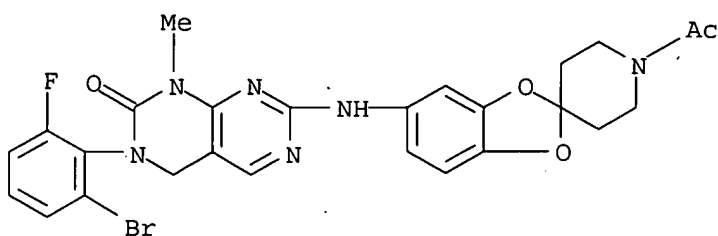
RN 686759-66-0 HCAPLUS

CN Spiro[1,3-benzodioxole-2,4'-piperidine]-1'-carboxylic acid, 5-[[6-(2-bromophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



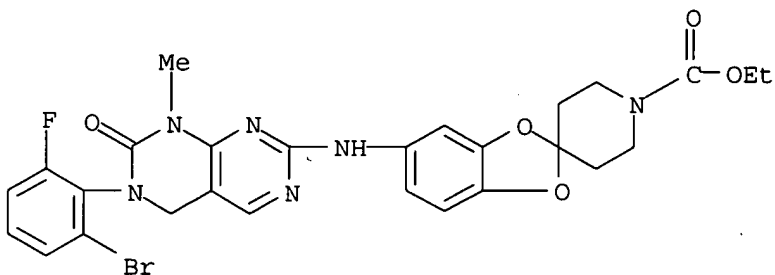
RN 686759-70-6 HCAPLUS

CN Spiro[1,3-benzodioxole-2,4'-piperidine], 1'-acetyl-5-[[6-(2-bromo-6-fluorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]- (9CI) (CA INDEX NAME)



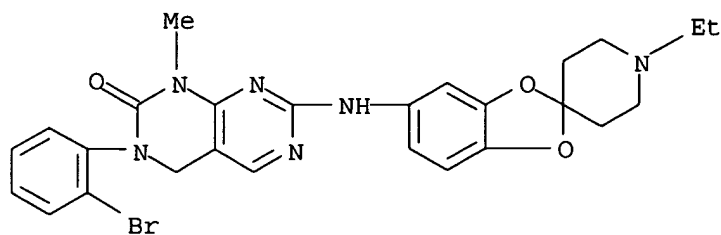
RN 686759-74-0 HCAPLUS

CN Spiro[1,3-benzodioxole-2,4'-piperidine]-1'-carboxylic acid, 5-[[6-(2-bromo-6-fluorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



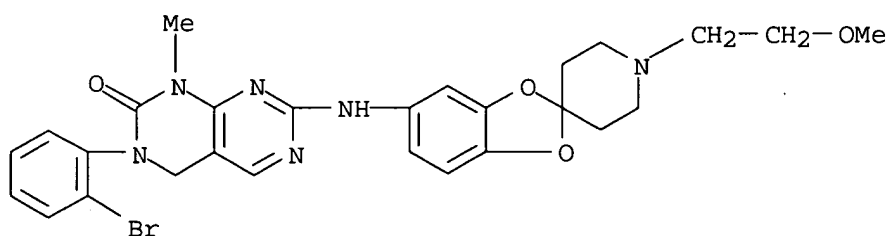
RN 686759-78-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[(1'-ethylspiro[1,3-benzodioxole-2,4'-piperidin]-5-yl)amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



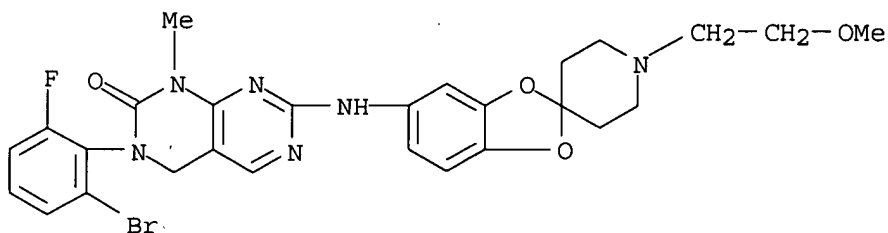
RN 686759-82-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-3,4-dihydro-7-[[1'-(2-methoxyethyl)spiro[1,3-benzodioxole-2,4'-piperidin]-5-yl]amino]-1-methyl- (9CI) (CA INDEX NAME)



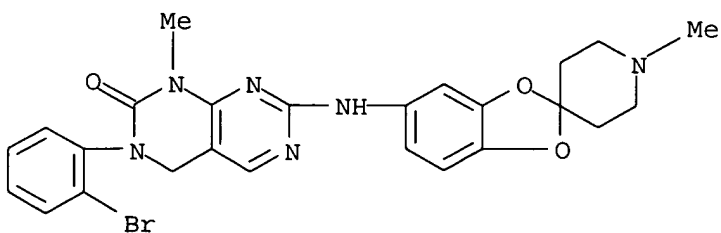
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CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromo-6-fluorophenyl)-3,4-dihydro-7-[[1'-(2-methoxyethyl)spiro[1,3-benzodioxole-2,4'-piperidin]-5-yl]amino]-1-methyl- (9CI) (CA INDEX NAME)



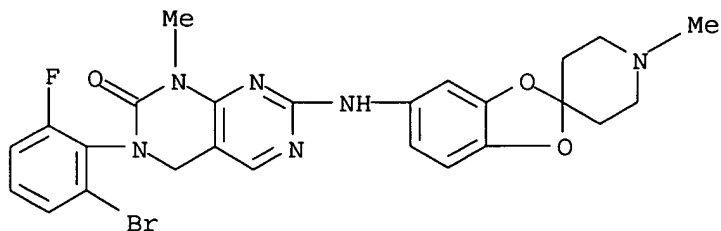
RN 686759-92-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-3,4-dihydro-1-methyl-7-[[1'-methylspiro[1,3-benzodioxole-2,4'-piperidin]-5-yl]amino]- (9CI) (CA INDEX NAME)



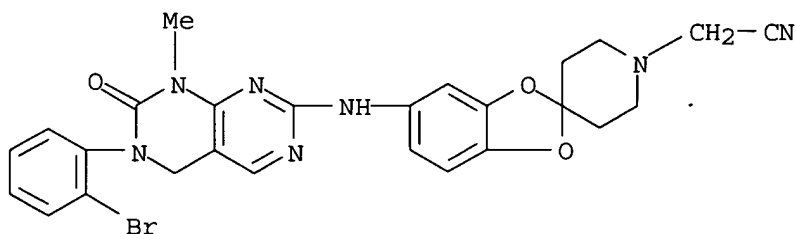
RN 686759-99-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromo-6-fluorophenyl)-3,4-dihydro-1-methyl-7-[(1'-methylspiro[1,3-benzodioxole-2,4'-piperidin]-5-yl)amino]-(9CI) (CA INDEX NAME)



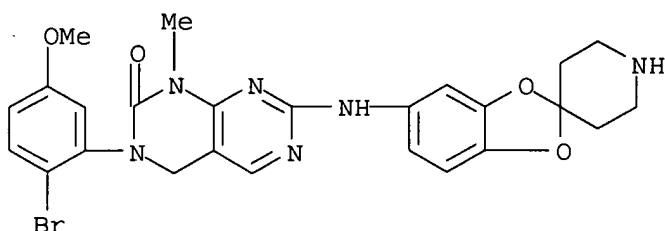
RN 686760-03-2 HCAPLUS

CN Spiro[1,3-benzodioxole-2,4'-piperidine]-1'-acetonitrile, 5-[[6-(2-bromophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-(9CI) (CA INDEX NAME)



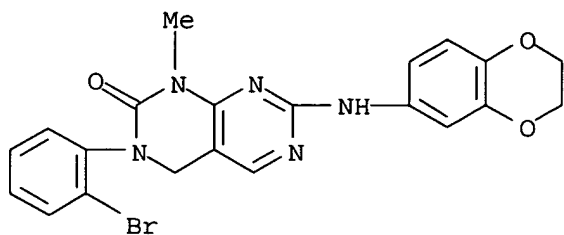
RN 686760-07-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromo-5-methoxyphenyl)-3,4-dihydro-1-methyl-7-(spiro[1,3-benzodioxole-2,4'-piperidin]-5-ylamino)-(9CI) (CA INDEX NAME)



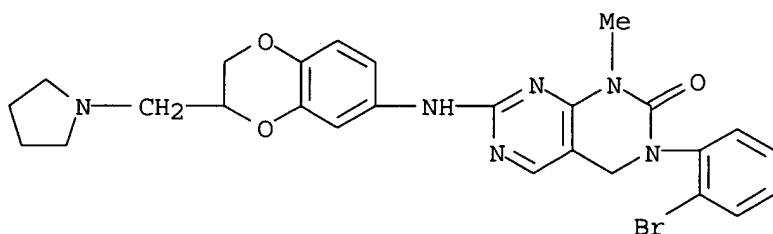
RN 686760-11-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[(2,3-dihydro-1,4-benzodioxin-6-yl)amino]-3,4-dihydro-1-methyl-(9CI) (CA INDEX NAME)



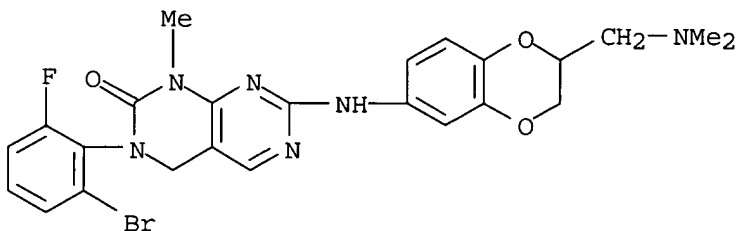
RN 686760-14-5 HCAPLUS

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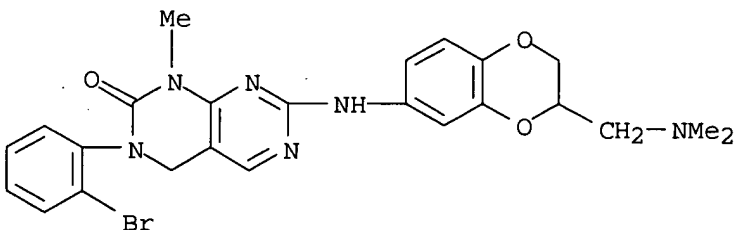
RN 686760-18-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromo-6-fluorophenyl)-7-[[2-[(dimethylamino)methyl]-2,3-dihydro-1,4-benzodioxin-6-yl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



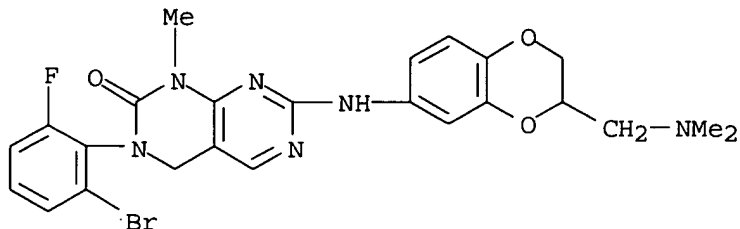
RN 686760-22-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[[3-[(dimethylamino)methyl]-2,3-dihydro-1,4-benzodioxin-6-yl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



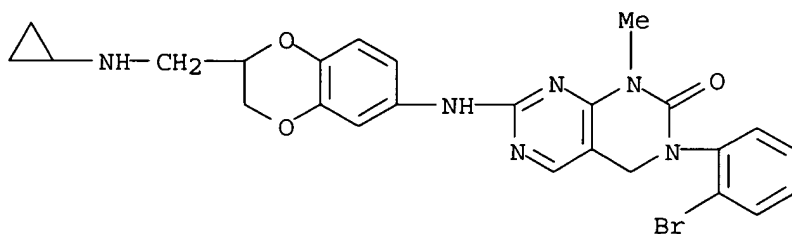
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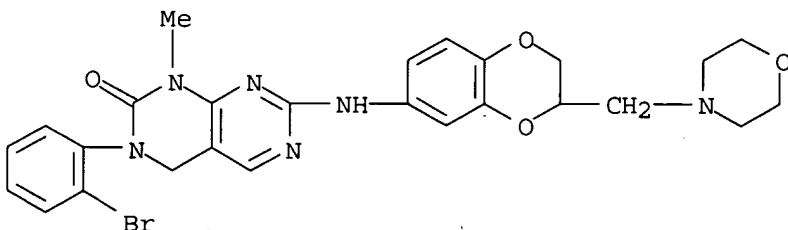
RN 686760-30-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[[2-[(cyclopropylamino)methyl]-2,3-dihydro-1,4-benzodioxin-6-yl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



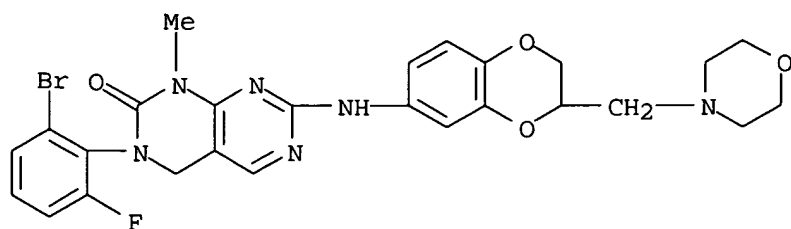
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CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[[2,3-dihydro-3-(4-morpholinylmethyl)-1,4-benzodioxin-6-yl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



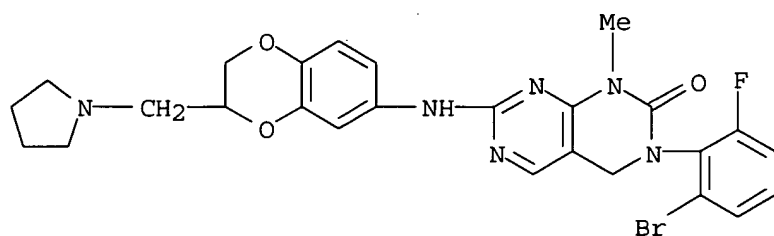
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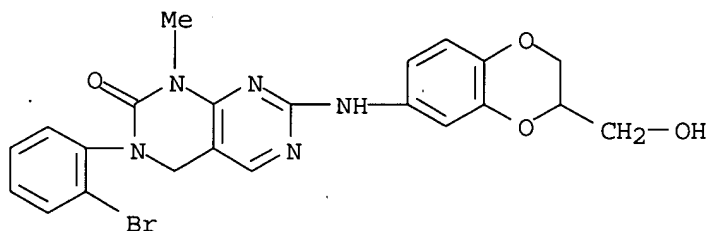
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CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromo-6-fluorophenyl)-7-[[2,3-dihydro-3-(1-pyrrolidinylmethyl)-1,4-benzodioxin-6-yl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



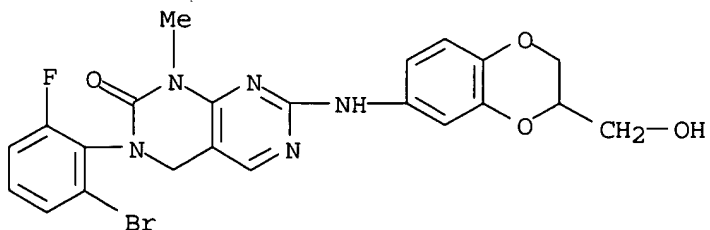
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CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[[2,3-dihydro-3-(hydroxymethyl)-1,4-benzodioxin-6-yl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



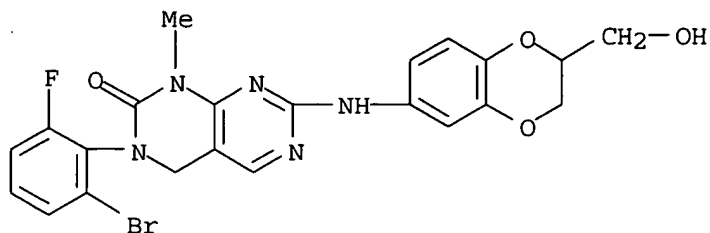
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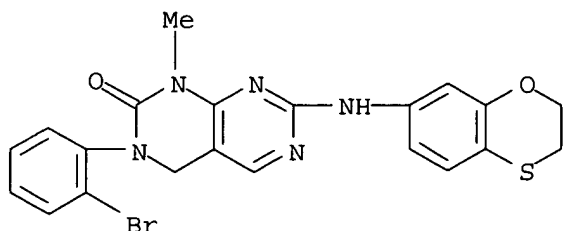
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CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromo-6-fluorophenyl)-7-[[2,3-dihydro-2-(hydroxymethyl)-1,4-benzodioxin-6-yl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



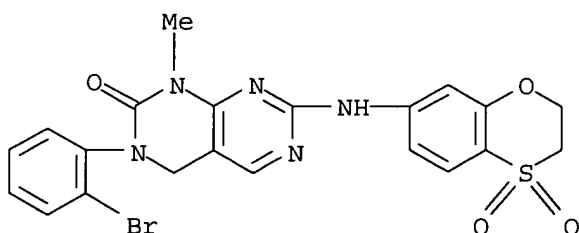
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CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[(2,3-dihydro-1,4-benzoxathiin-7-yl)amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



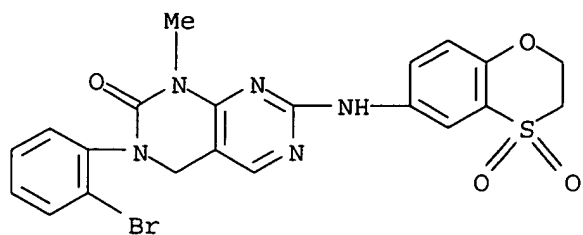
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CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[(2,3-dihydro-4,4-dioxido-1,4-benzoxathiin-7-yl)amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



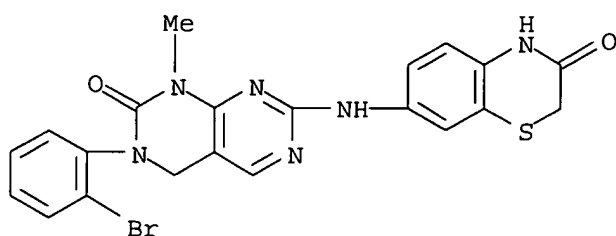
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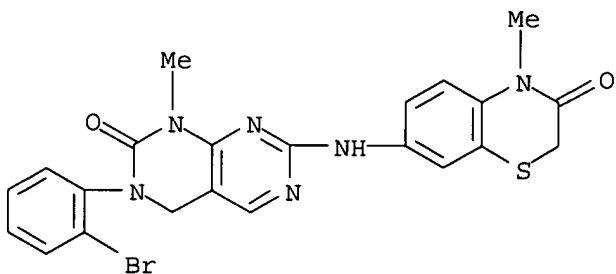
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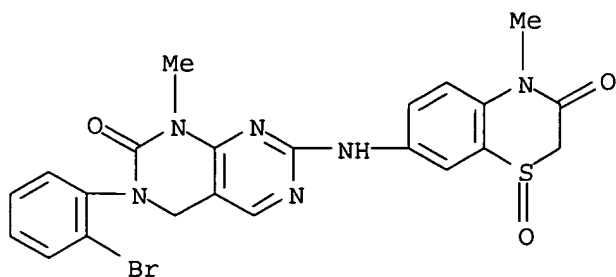
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CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[(3,4-dihydro-4-methyl-3-oxo-2H-1,4-benzothiazin-7-yl)amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



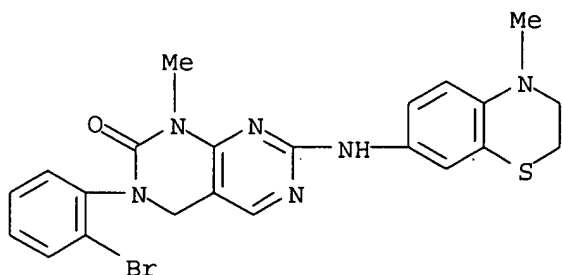
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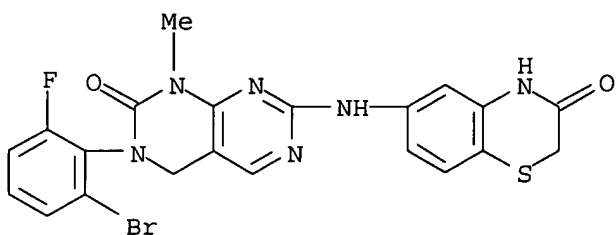
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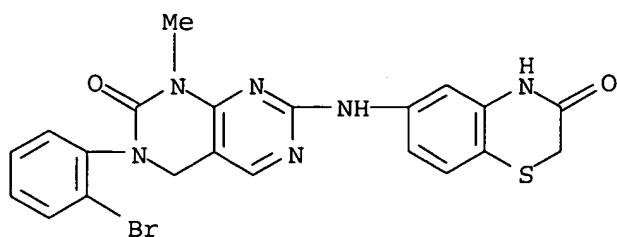
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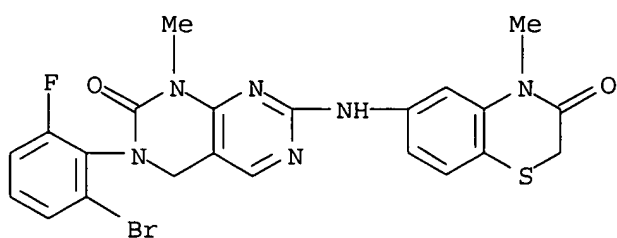
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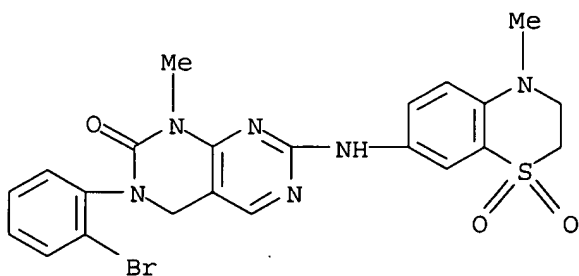
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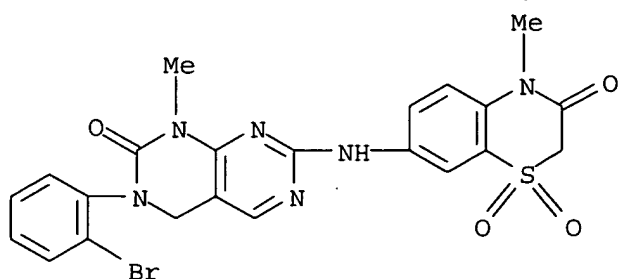
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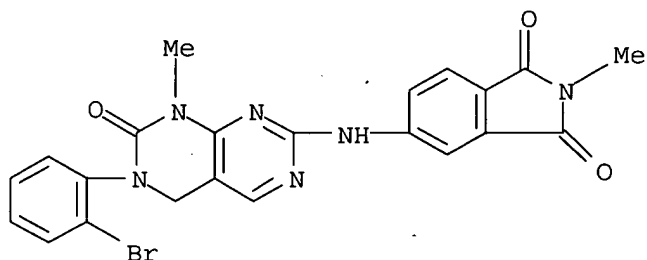
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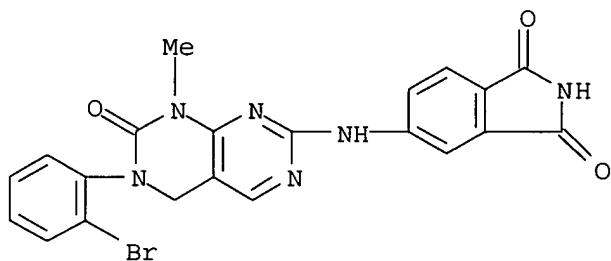
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CN 1H-Isoindole-1,3(2H)-dione, 5-[[6-(2-bromophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-2-methyl- (9CI) (CA INDEX NAME)



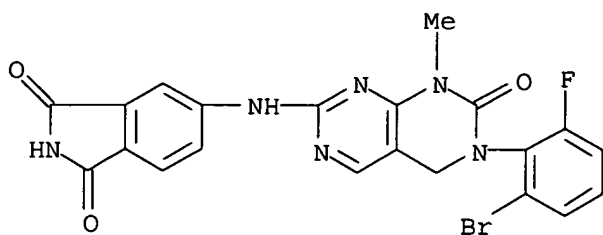
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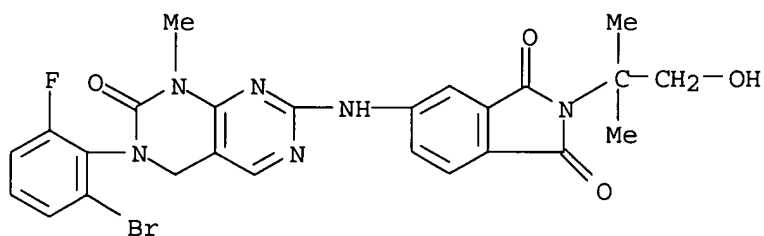
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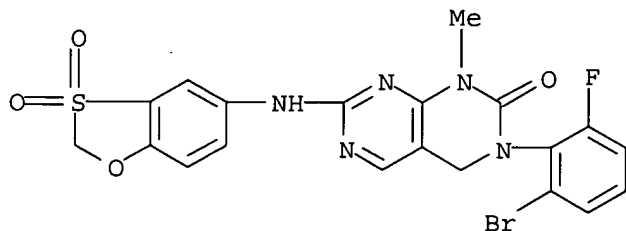
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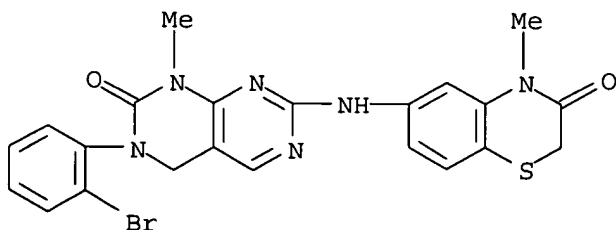
RN 686761-36-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromo-6-fluorophenyl)-7-[(3,3-dioxido-1,3-benzoxathiol-5-yl)amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 686766-23-4 HCAPLUS

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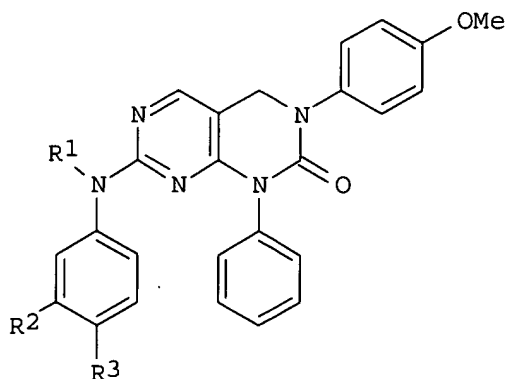


L27 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2004:162462 HCAPLUS
 DOCUMENT NUMBER: 140:199340
 TITLE: Preparation of pyrimidopyrimidinone derivatives having antiproliferative activity
 INVENTOR(S): Chen, Yi; Daniewski, Andrzej Robert; Harris, William; Kabat, Marek Michal; Liu, Emily Aijun; Liu, Jin-jun; Luk, Kin-chun; Michoud, Christophe
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 25 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2004038995 | A1 | 20040226 | US 2003-623972 | 20030721 |
| WO 2004018472 | A2 | 20040304 | WO 2003-EP8744 | 20030807 |
| WO 2004018472 | A3 | 20040429 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-403519P P 20020814
 OTHER SOURCE(S): MARPAT 140:199340
 GI



I

AB The title I [R1 = H, COR4, COOCHR5OCOR4; R2,R3 = H or OR5; R4 = alkyl, or alkyl substituted by NR5R6, SR5, OR5, (substituted)aryl, heteroaryl, heterocycle; R5, R6 = H, alkyl or NR5R6 form a ring optionally including one or more addnl. N or O] were prepared as selective inhibitors of both KDR

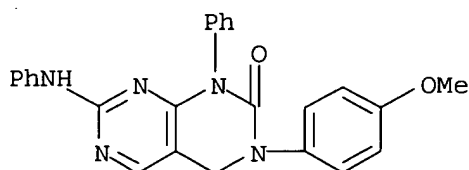
and FGFR kinases and are selective against LCK. Thus, reaction of 7-chloro-3-(4-methoxyphenyl)-1-phenyl-1,3,4-trihydropyrimidino[4,5-d]-2-one (preparation given) with aniline yielded compound II (R1, R2, R3 = H). The latter showed inhibition of KDR, FGFR, EGFR and PDGFR with IC50 = 0.044, 0.076, 0.360, and 0.130 μ M, resp.

IT **663198-02-5P 663198-20-7P 663198-33-2P**

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyrimidopyrimidinone derivs. having antiproliferative activity)

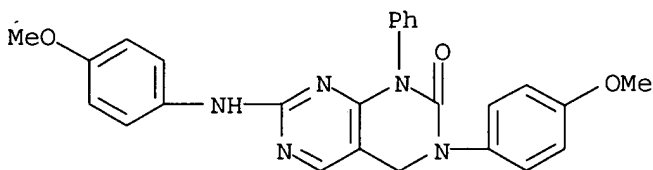
RN 663198-02-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-3-(4-methoxyphenyl)-1-phenyl-7-(phenylamino)- (9CI) (CA INDEX NAME)



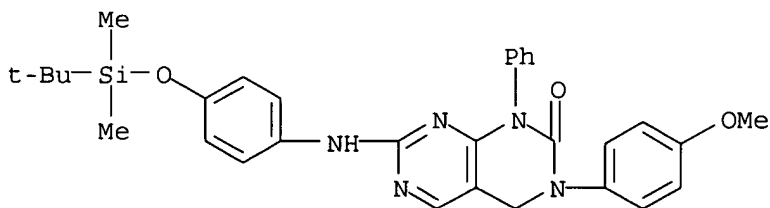
RN 663198-20-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-3-(4-methoxyphenyl)-7-[(4-methoxyphenyl)amino]-1-phenyl- (9CI) (CA INDEX NAME)



RN 663198-33-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]phenyl]amino]-3,4-dihydro-3-(4-methoxyphenyl)-1-phenyl- (9CI) (CA INDEX NAME)

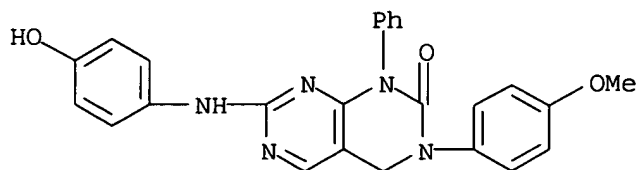


IT **663198-18-3P 663198-22-9P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrimidopyrimidinone derivs. having antiproliferative activity)

RN 663198-18-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-7-[(4-hydroxyphenyl)amino]-3-(4-methoxyphenyl)-1-phenyl- (9CI) (CA INDEX NAME)



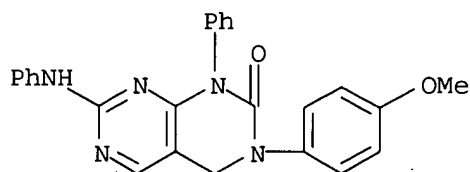
RN 663198-22-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-3-(4-methoxyphenyl)-1-phenyl-7-(phenylamino)-, mono(methanesulfonate) (9CI) (CA INDEX NAME)

CM 1

CRN 663198-02-5

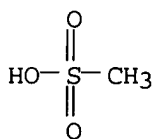
CMF C25 H21 N5 O2



CM 2

CRN 75-75-2

CMF C H4 O3 S



L27 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:80385 HCAPLUS

DOCUMENT NUMBER: 140:146153

TITLE: Preparation of pyrimidopyrimidinones as kinase inhibitors

INVENTOR(S): Chivikas, Connolly Cleo J.; Deur, Christopher James; Hamby, James Marino; Hoyer, Denton Wade; Limberakis, Chris; Reed, Jessica Elizabeth; Schroeder, Mel Conrad; Taylor, Clarke

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 44 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

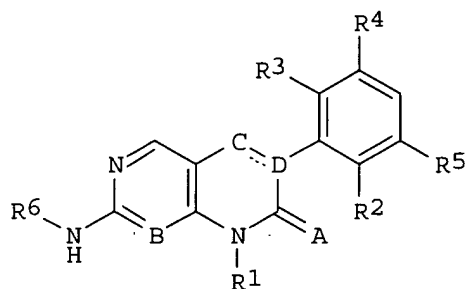
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

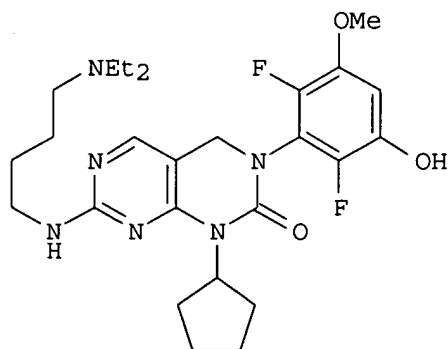
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| US 2004019210 | A1 | 20040129 | US 2003-621983 | 20030717 |
| CA 2493633 | AA | 20040205 | CA 2003-2493633 | 20030721 |
| WO 2004011465 | A1 | 20040205 | WO 2003-IB3359 | 20030721 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRIORITY APPLN. INFO.: | | | US 2002-398638P | P 20020725 |
| | | | WO 2003-IB3359 | W 20030721 |

OTHER SOURCE(S): MARPAT 140:146153
GI



I



II

AB This invention provides phenyl-substituted pyrimidopyrimidines, dihydropyrimidopyrimidines, pyridopyrimidines, naphthyridines, and pyridopyrazines of the general formula I [A = O, NH₂, mono(or di)alkylamino, NHCONHR₁₂ (wherein R₁₂ = alkyl, alkylencycloalkyl); B, C, D = CH, N (with the proviso that C and D are not both N); R₁ = alkyl

(optionally substituted by CO₂H), (un)substituted Ph, CH₂Ph, piperidiny1, etc.; R₂ = H, Cl, F; R₃ = H, Cl, F (at least one of R₂ or R₃ = F); R₄ = H, OH, OMe, OEt (if R₄ = H, R₂ and R₃ is not H); R₅ = OMe, OEt; R₆ = H, alkyl-NH₂, O-alkyl-NH₂, etc.] that inhibit cyclin-dependent kinase and tyrosine kinase enzymes, methods and intermediates for their synthesis, as well as pharmaceutical compns. and methods for their use in treating, inhibiting or preventing maladies associated with cell proliferative disorders, including angiogenesis, atherosclerosis, restenosis, and cancer (no biol. data given). Synthesis of 35 title compds. I is described. E.g., a multi-step synthesis of II was given.

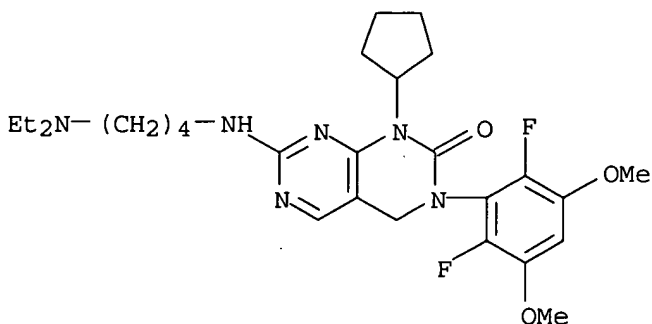
IT 651734-15-5P 651734-16-6P 651734-35-9P

651734-43-9P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyrimidopyrimidinones as kinase inhibitors)

RN 651734-15-5 HCAPLUS

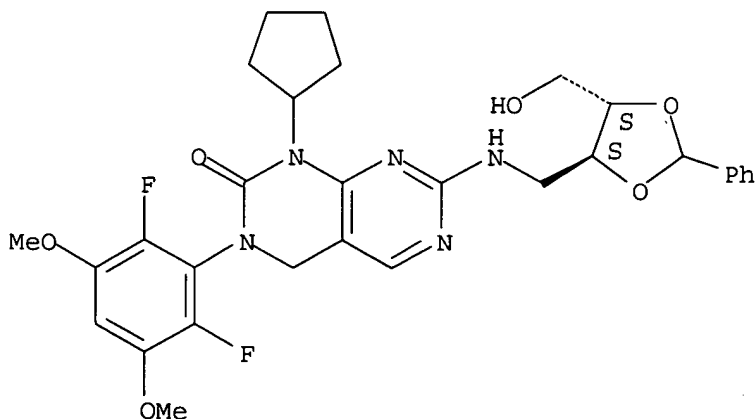
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-7-[[4-(diethylamino)butyl]amino]-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)



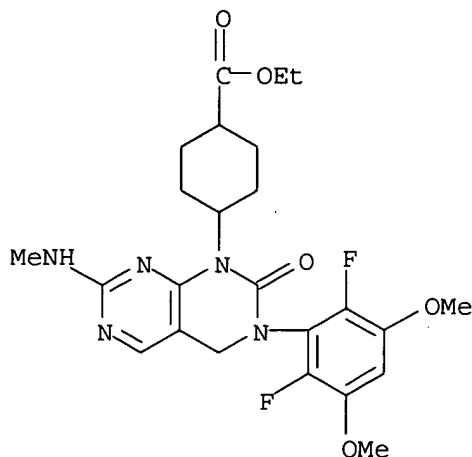
RN 651734-16-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[[[(4S,5S)-5-(hydroxymethyl)-2-phenyl-1,3-dioxolan-4-yl]methyl]amino]- (9CI) (CA INDEX NAME)

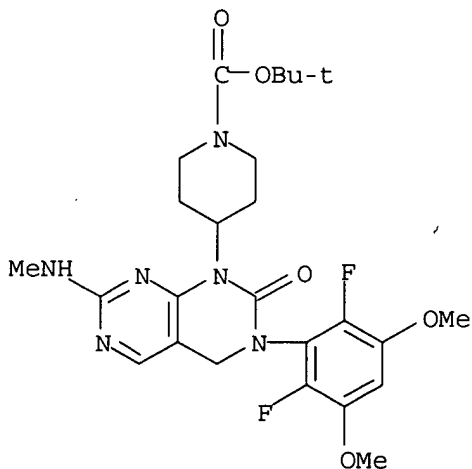
Absolute stereochemistry.



RN 651734-35-9 HCAPLUS
 CN Cyclohexanecarboxylic acid, 4-[3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 651734-43-9 HCAPLUS
 CN 1-Piperidinecarboxylic acid, 4-[3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



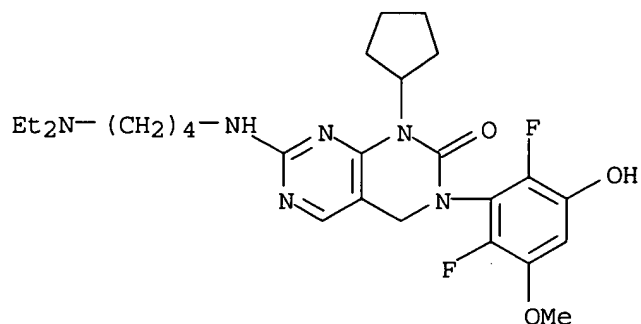
IT 651734-14-4P 651734-17-7P 651734-18-8P
 651734-19-9P 651734-20-2P 651734-21-3P
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 651734-25-7P 651734-26-8P 651734-27-9P
 651734-28-0P 651734-29-1P 651734-30-4P
 651734-31-5P 651734-32-6P 651734-33-7P
 651734-34-8P 651734-36-0P 651734-38-2P
 651734-39-3P 651734-40-6P 651734-41-7P
 651734-42-8P 651734-45-1P 651734-46-2P
 651734-47-3P 651734-48-4P 651734-49-5P
 651734-50-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrimidopyrimidinones as kinase inhibitors)

RN 651734-14-4 HCAPLUS

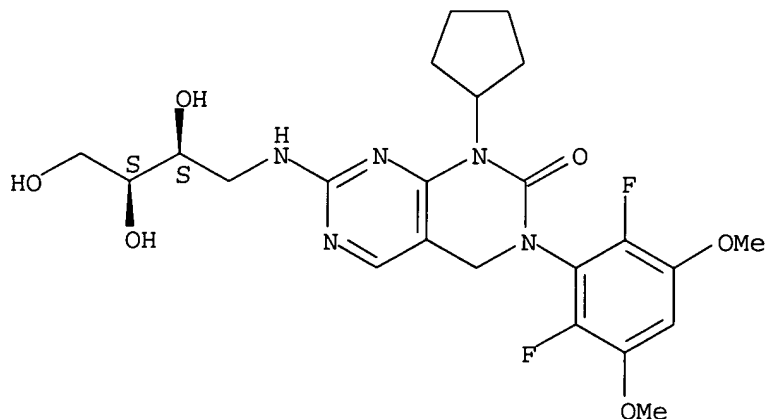
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-7-[[4-(diethylamino)butyl]amino]-3-(2,6-difluoro-3-hydroxy-5-methoxyphenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 651734-17-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[[2,3,4-trihydroxybutyl]amino]- (9CI) (CA INDEX NAME)

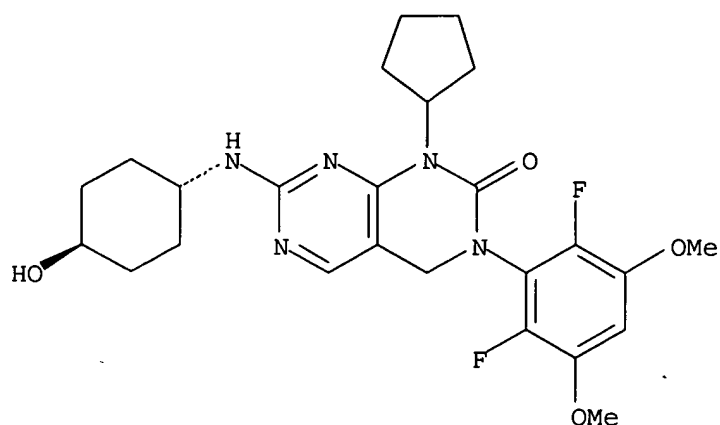
Absolute stereochemistry.



RN 651734-18-8 HCAPLUS

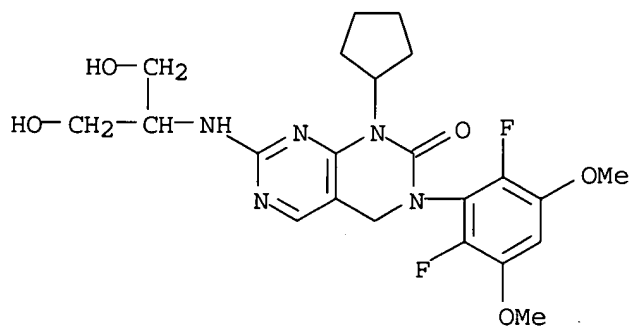
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



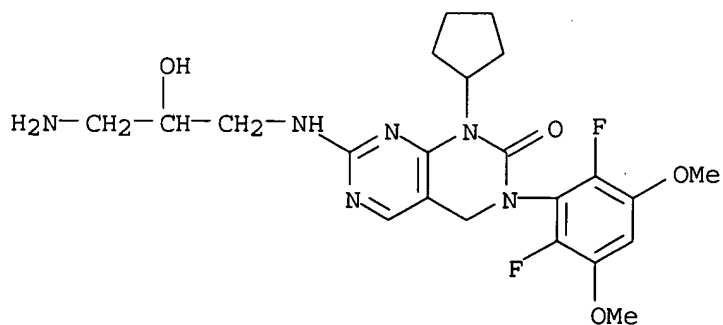
RN 651734-19-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino] - (9CI) (CA INDEX NAME)



RN 651734-20-2 HCAPLUS

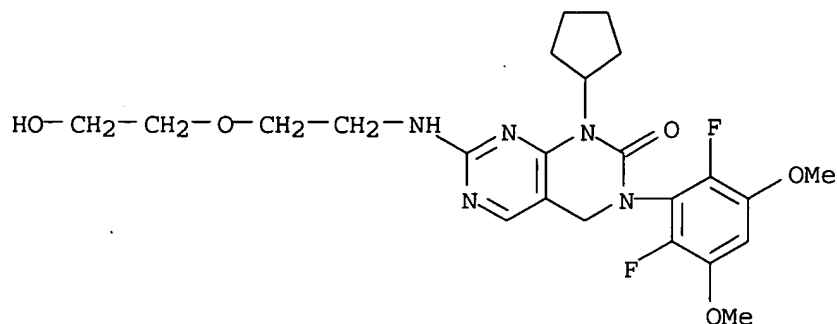
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(3-amino-2-hydroxypropyl)amino]-1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 651734-21-3 HCAPLUS

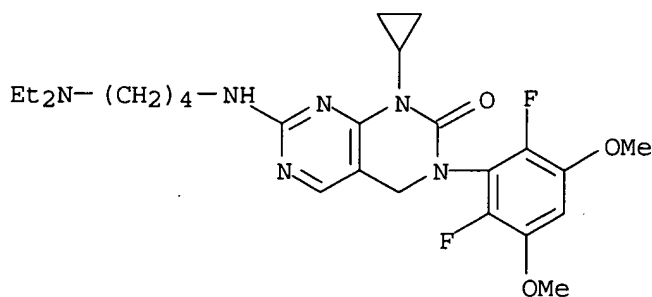
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[[2-(2-hydroxyethoxy)ethyl]amino] - (9CI)

(CA INDEX NAME)



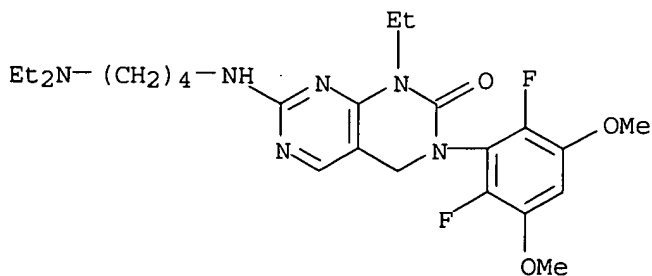
RN 651734-22-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-7-[[4-(diethylamino)butyl]amino]-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)



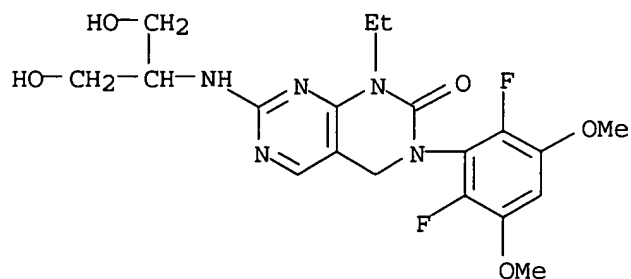
RN 651734-23-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[4-(diethylamino)butyl]amino]-3-(2,6-difluoro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 651734-24-6 HCAPLUS

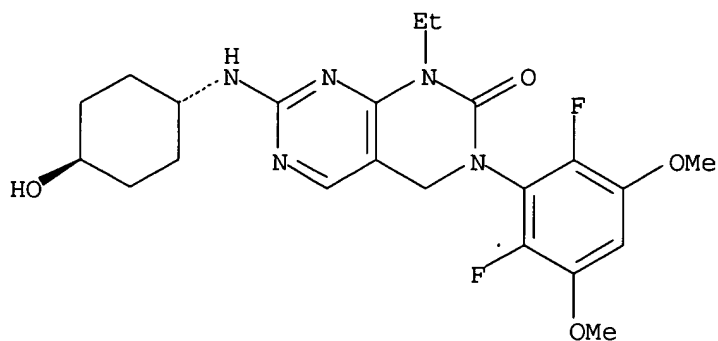
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-difluoro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro-7-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]- (9CI) (CA INDEX NAME)



RN 651734-25-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-difluoro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]- (9CI) (CA INDEX NAME)

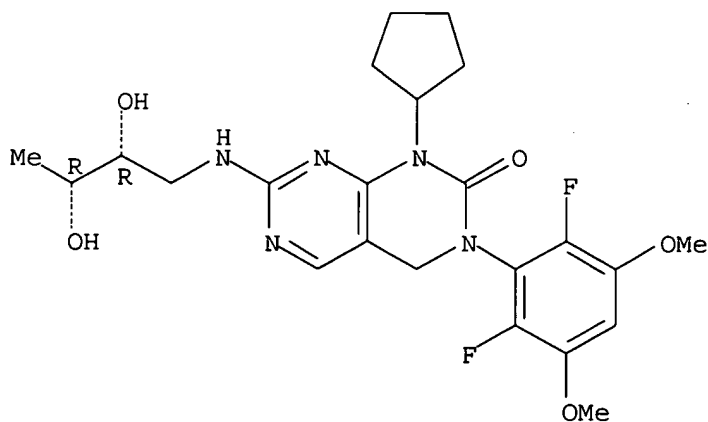
Relative stereochemistry.



RN 651734-26-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-7-[[[(2R,3R)-2,3-dihydroxybutyl]amino]-3,4-dihydro- (9CI) (CA INDEX NAME)

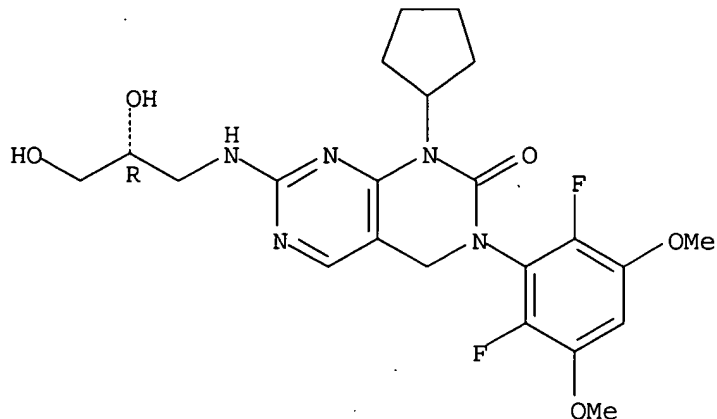
Absolute stereochemistry.



RN 651734-27-9 HCAPLUS

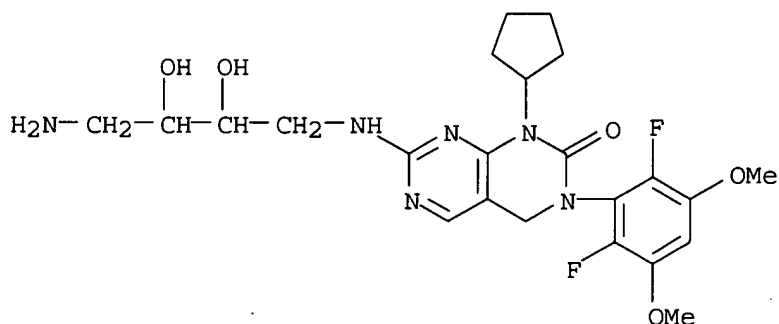
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-7-[[(2R)-2,3-dihydroxypropyl]amino]-3,4-dihydro- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 651734-28-0 HCAPLUS

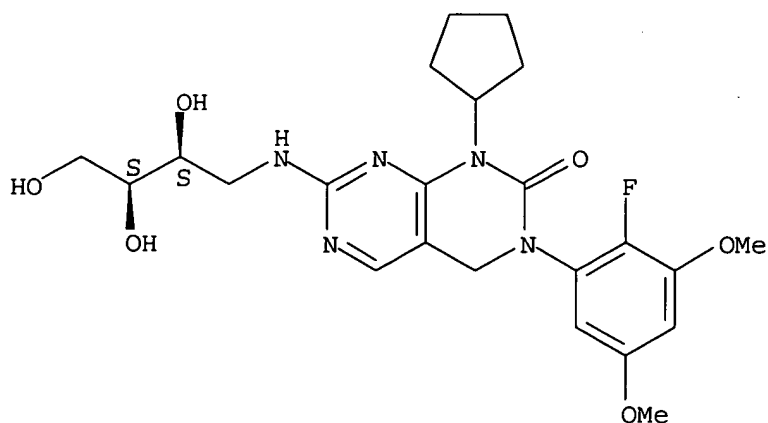
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(4-amino-2,3-dihydroxybutyl)amino]-1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 651734-29-1 HCAPLUS

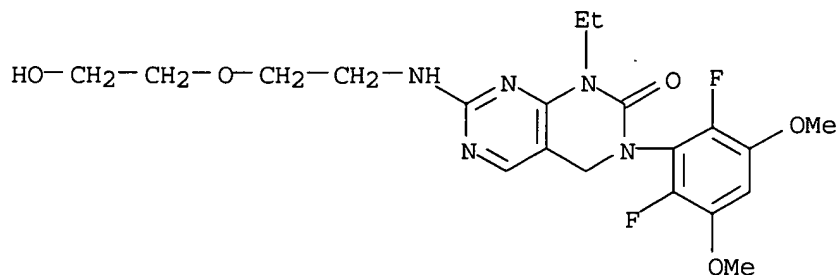
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2-fluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[[(2S,3S)-2,3,4-trihydroxybutyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 651734-30-4 HCAPLUS

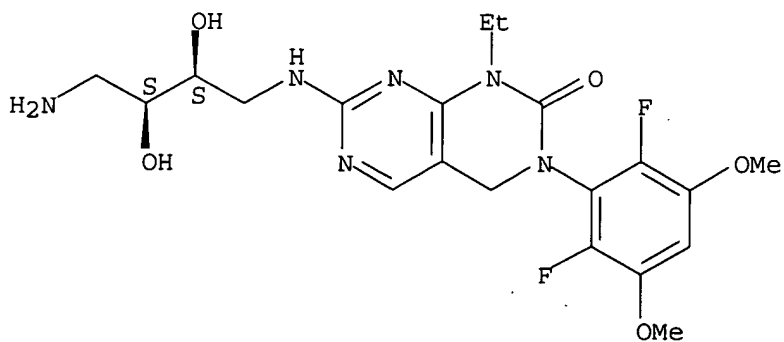
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-difluoro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro-7-[[2-(2-hydroxyethoxy)ethyl]amino]- (9CI) (CA INDEX NAME)



RN 651734-31-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[[(2S,3S)-4-amino-2,3-dihydroxybutyl]amino]-3-(2,6-difluoro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)

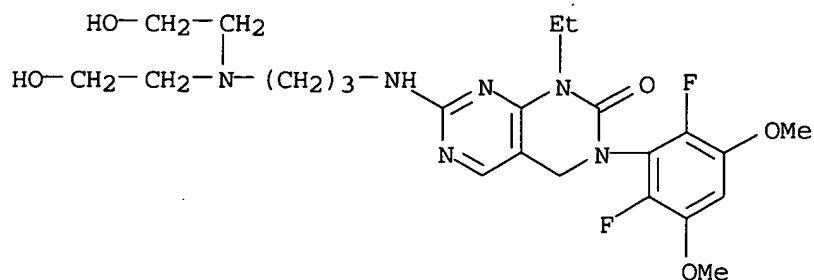
Absolute stereochemistry.



RN 651734-32-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[3-[bis(2-

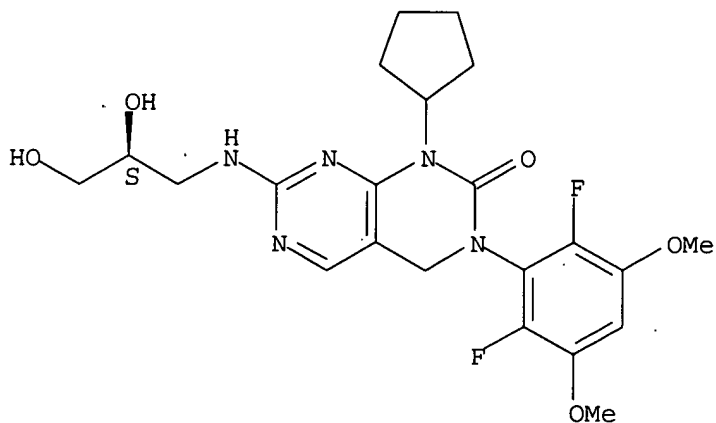
hydroxyethyl)amino]propyl]amino]-3-(2,6-difluoro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 651734-33-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-difluoro-3,5-dimethoxyphenyl)-7-[[(2S)-2,3-dihydroxypropyl]amino]-3,4-dihydro- (9CI) (CA INDEX NAME)

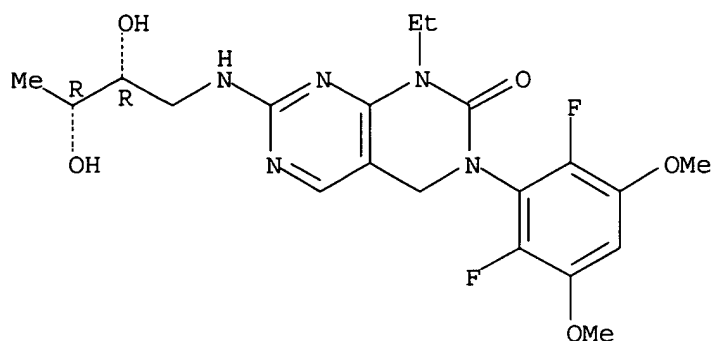
Absolute stereochemistry.



RN 651734-34-8 HCAPLUS

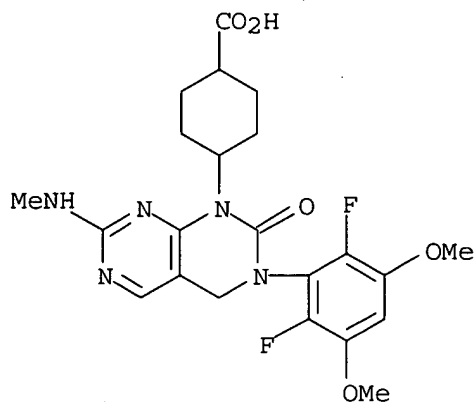
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-difluoro-3,5-dimethoxyphenyl)-7-[[(2R,3R)-2,3-dihydroxybutyl]amino]-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 651734-36-0 HCAPLUS

CN Cyclohexanecarboxylic acid, 4-[3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylamino)-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]- (9CI)
(CA INDEX NAME)



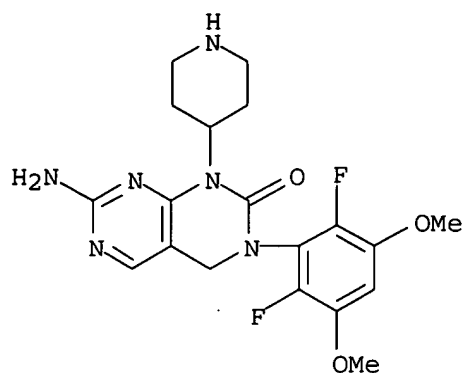
RN 651734-38-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-amino-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-1-(4-piperidinyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 651734-37-1

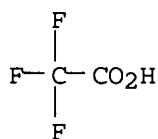
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CM 2

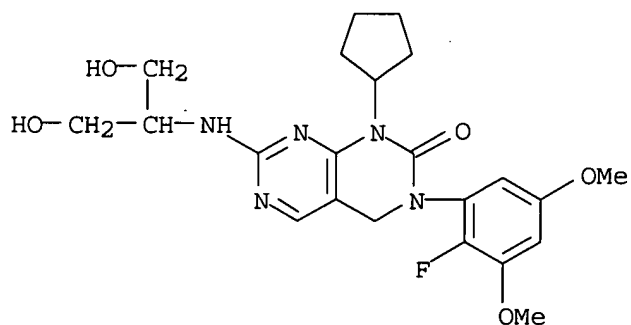
CRN 76-05-1

CMF C2 H F3 O2



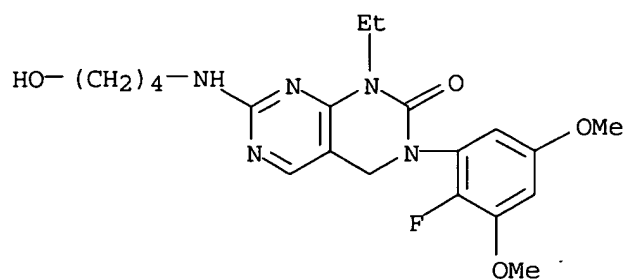
RN 651734-39-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2-fluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino] - (9CI) (CA INDEX NAME)



RN 651734-40-6 HCAPLUS

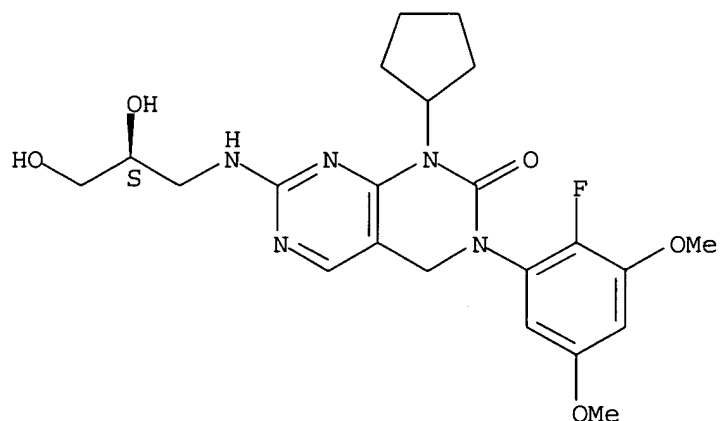
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-ethyl-3-(2-fluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[(4-hydroxybutyl)amino] - (9CI) (CA INDEX NAME)



RN 651734-41-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-7-[[(2S)-2,3-dihydroxypropyl]amino]-3-(2-fluoro-3,5-dimethoxyphenyl)-3,4-dihydro- (9CI)
(CA INDEX NAME)

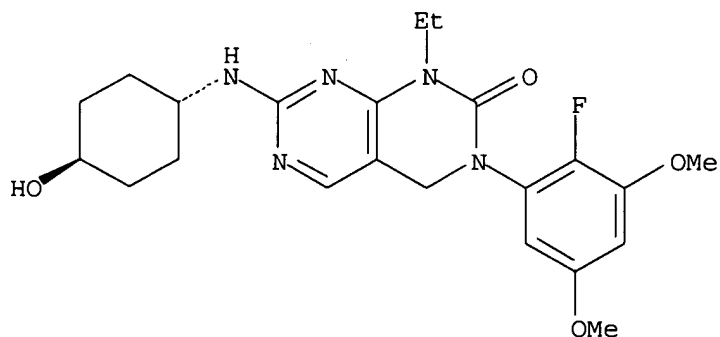
Absolute stereochemistry.



RN 651734-42-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-fluoro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



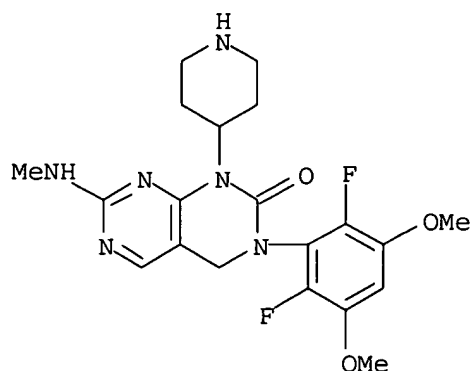
RN 651734-45-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(methylamino)-1-(4-piperidinyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 651734-44-0

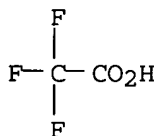
CMF C20 H24 F2 N6 O3



CM 2

CRN 76-05-1

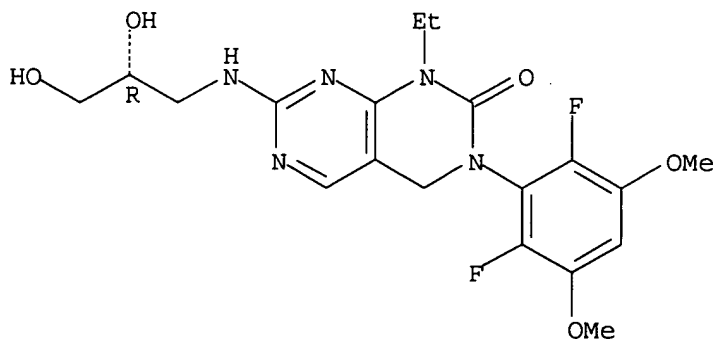
CMF C2 H F3 O2



RN 651734-46-2 HCAPLUS

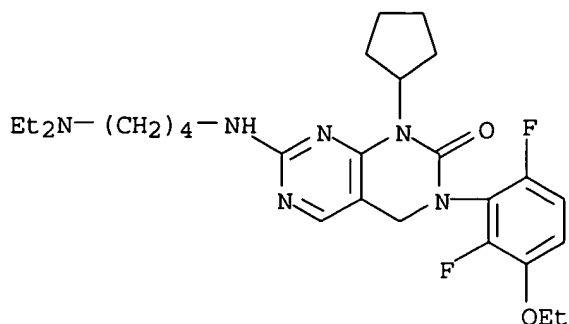
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-difluoro-3,5-dimethoxyphenyl)-7-[[(2R)-2,3-dihydroxypropyl]amino]-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 651734-47-3 HCAPLUS

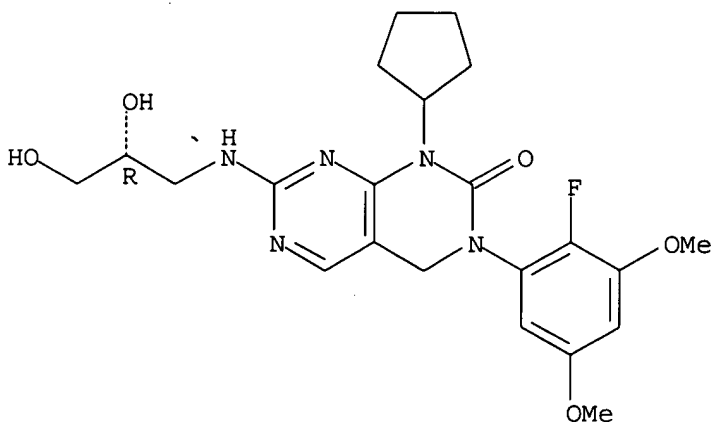
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-7-[[4-(diethylamino)butyl]amino]-3-(3-ethoxy-2,6-difluorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 651734-48-4 HCAPLUS

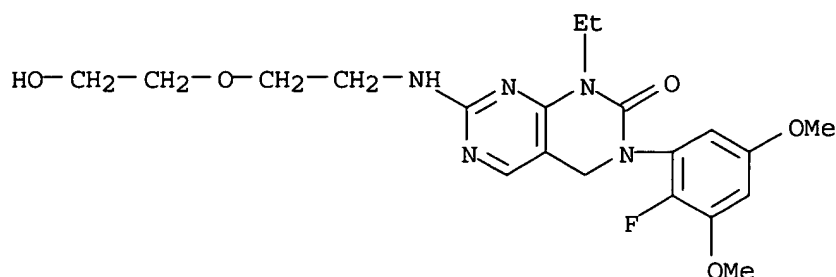
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-7-[[(2R)-2,3-dihydroxypropyl]amino]-3-(2-fluoro-3,5-dimethoxyphenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 651734-49-5 HCAPLUS

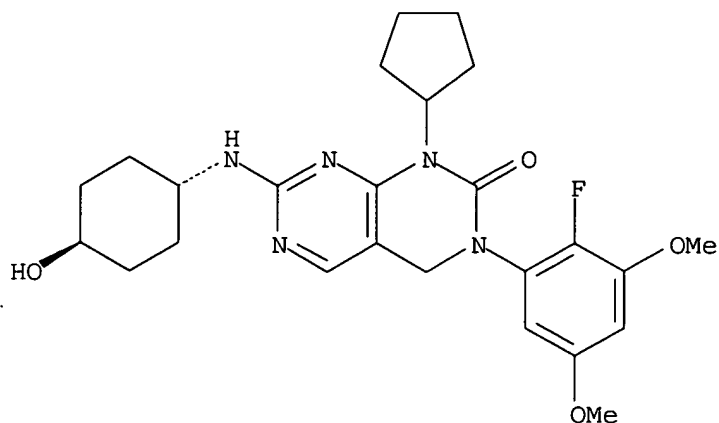
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-ethyl-3-(2-fluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[[2-(2-hydroxyethoxy)ethyl]amino]- (9CI) (CA INDEX NAME)



RN 651734-50-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2-fluoro-3,5-dimethoxyphenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]- (9CI)
(CA INDEX NAME)

Relative stereochemistry.

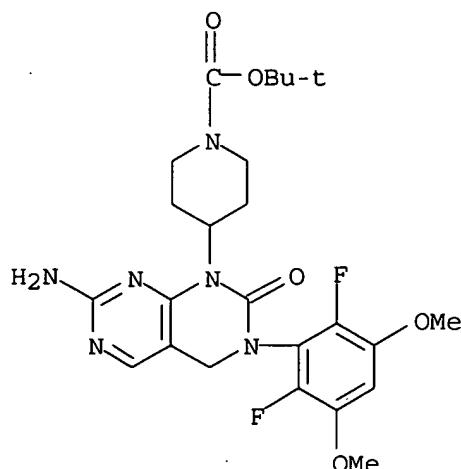


IT **651735-18-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of pyrimidopyrimidinones as kinase inhibitors)

RN 651735-18-1 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[7-amino-3-(2,6-difluoro-3,5-dimethoxyphenyl)-3,4-dihydro-2-oxypyrimido[4,5-d]pyrimidin-1(2H)-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L27 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:651919 HCAPLUS

DOCUMENT NUMBER: 140:16695

TITLE: Solid-phase synthesis of pyrimido[4,5-d]pyrimidine-2,4(1H,3H)-diones

AUTHOR(S): Graveleau, Nadege; Masquelin, Thierry

CORPORATE SOURCE: Combinatorial & Parallel Chemistry, Basilea Pharmaceutica Ltd., Basel, 4002, Switz.

SOURCE: Synthesis (2003), (11), 1739-1743

CODEN: SYNTBF; ISSN: 0039-7881

PUBLISHER: Georg Thieme Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 140:16695

AB The authors report a novel and versatile solid-phase synthesis of pyrimido[4,5-d]pyrimidine-2,4(1H,3H)-diones starting from the polymer-bound Et 4-amino-2-sulfanylpurimidine-5-carboxylate. The key step is based on the reaction of the support-bound pyrimidine with isocyanates, involving formation of a carbamate intermediate, followed by a base-catalyzed intramol. ring closure, to give polymer-bound 3-monosubstituted 1H-pyrimido[4,5-d]pyrimidine-2,4(1H,3H)-diones. At this stage, subsequent treatment with alkyl halides led to 1,3-disubstituted 2H-pyrimido[4,5-d]pyrimidine-2,4(1H,3H)-dione intermediates, which after oxidation and cleavage with various amines gave 1,3-disubstituted 7-amino-2H-pyrimido[4,5-d]pyrimidine-2,4(1H,3H)-diones in moderate yields and high purity.

IT 630394-21-7P 630394-23-9P 630394-24-0P

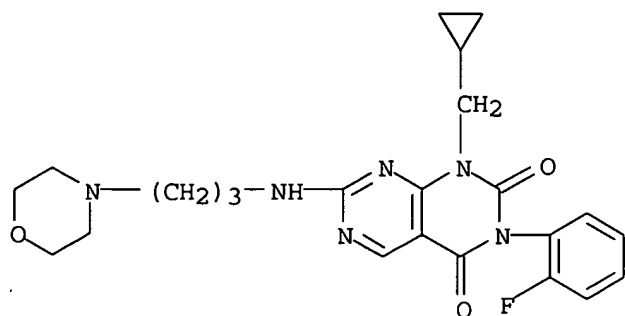
630394-25-1P

RL: SPN (Synthetic preparation); PREP (Preparation)

(solid-phase synthesis of pyrimido[4,5-d]pyrimidine-2,4(1H,3H)-diones)

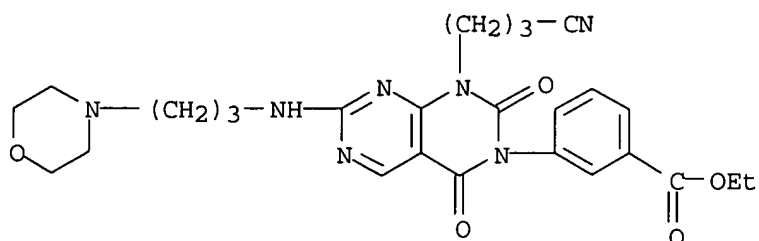
RN 630394-21-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-2,4(1H,3H)-dione, 1-(cyclopropylmethyl)-3-(2-fluorophenyl)-7-[[3-(4-morpholinyl)propyl]amino]- (9CI) (CA INDEX NAME)



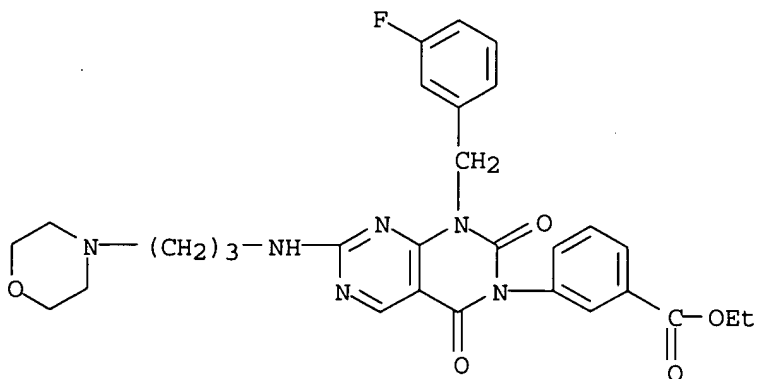
RN 630394-23-9 HCAPLUS

CN Benzoic acid, 3-[1-(3-cyanopropyl)-1,4-dihydro-7-[[3-(4-morpholinyl)propyl]amino]-2,4-dioxypyrimido[4,5-d]pyrimidin-3(2H)-yl]-, ethyl ester (9CI) (CA INDEX NAME)



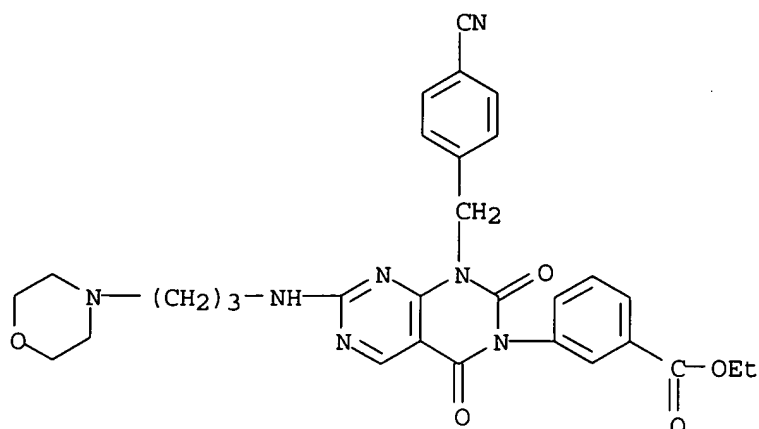
RN 630394-24-0 HCAPLUS

CN Benzoic acid, 3-[1-[(3-fluorophenyl)methyl]-1,4-dihydro-7-[[3-(4-morpholinyl)propyl]amino]-2,4-dioxypyrimido[4,5-d]pyrimidin-3(2H)-yl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 630394-25-1 HCAPLUS

CN Benzoic acid, 3-[1-[(4-cyanophenyl)methyl]-1,4-dihydro-7-[[3-(4-morpholinyl)propyl]amino]-2,4-dioxypyrimido[4,5-d]pyrimidin-3(2H)-yl]-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:300721 HCAPLUS

DOCUMENT NUMBER: 134:326540

TITLE: Preparation of alkylamino substituted bicyclic nitrogen heterocycles for pharmaceutical use as inhibitors of p38 protein kinase

INVENTOR(S): Dunn, James Patrick; Fisher, Lawrence Emerson; Goldstein, David Michael; Harris, William; Hill, Christopher Huw; Smith, Ian Edward David; Welch, Teresa Rosanne

PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.

SOURCE: PCT Int. Appl., 177 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

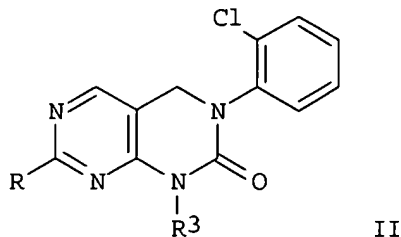
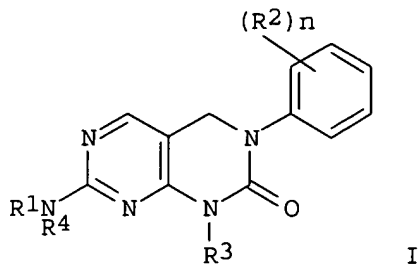
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|----------|
| WO 2001029042 | A1 | 20010426 | WO 2000-EP10088 | 20001013 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2388142 | AA | 20010426 | CA 2000-2388142 | 20001013 |
| BR 2000015243 | A | 20020716 | BR 2000-15243 | 20001013 |
| EP 1228070 | A1 | 20020807 | EP 2000-967864 | 20001013 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| TR 200201057 | T2 | 20020923 | TR 2002-200201057 | 20001013 |
| JP 2003512378 | T2 | 20030402 | JP 2001-531840 | 20001013 |
| NZ 518119 | A | 20040227 | NZ 2000-518119 | 20001013 |

| | | | | |
|------------------------|-------------------|----------|-----------------|------------|
| AU 776250 | B2 | 20040902 | AU 2000-77873 | 20001013 |
| US 6451804 | B1 | 20020917 | US 2000-693337 | 20001020 |
| ZA 2002002540 | A | 20030630 | ZA 2002-2540 | 20020328 |
| NO 2002001781 | A | 20020418 | NO 2002-1781 | 20020416 |
| PRIORITY APPLN. INFO.: | | | US 1999-160803P | P 19991021 |
| | | | US 2000-213743P | P 20000622 |
| | | | WO 2000-EP10088 | W 20001013 |
| OTHER SOURCE(S): | MARPAT 134:326540 | | | |
| GI | | | | |



AB Alkylamino-substituted dihydropyrimido[4,5-d]pyrimidinone derivs., such as I [R1 = H, alkyl, alkenyl, alkynyl, acyl, cycloalkyl, etc.; R2 = vinyl, alkyl, halogen, heteroalkyl; R3 = alkyl, heteroalkyl, cycloalkyl, heterocyclyl, etc.; R4 = H, alkyl, etc.; n = 0-3], were prepared for pharmaceutical use. The compds. are p38 inhibitors and may be used in the treatment of arthritis, Crohn's disease, irritable bowel syndrome, adult respiratory distress syndrome, chronic obstructive pulmonary disease, osteoporosis, or Alzheimer's disease. Thus, dihydropyrimido[4,5-d]pyrimidinone II (R = NHCMe2CH2OH, R3 = Me) was prepared via a substitution reaction of H2NCMe2CH2OH with sulfone II (R = SO2Me, R3 = Me) when combined and heated to 100-110° for 1 h. The prepared dihydropyrimido[4,5-d]pyrimidinone derivs. showed 50% p38 inhibitory activity at concns. < 10 µM.

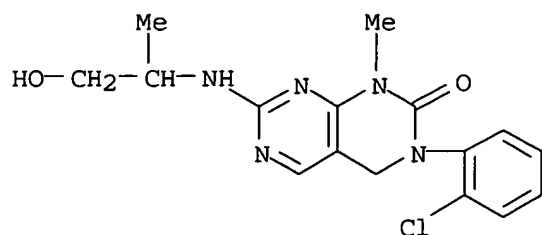
IT 335651-19-9P 335651-20-2P 335651-24-6P
 335651-30-4P 335651-49-5P 335651-50-8P
 335651-53-1P 335651-55-3P 335651-56-4P
 335651-57-5P 335651-58-6P 335651-61-1P
 335651-77-9P 335651-88-2P 335651-89-3P
 335651-93-9P 335651-94-0P 335651-95-1P
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 335652-14-7P 335652-16-9P 335652-18-1P
 335652-22-7P 335652-24-9P 335652-26-1P
 335652-30-7P 335652-32-9P 335652-36-3P
 335652-39-6P 335652-40-9P 335652-41-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of alkylamino substituted pyrimidino[4,5-d]pyrimidines for pharmaceutical use as inhibitors of p38 protein kinase)

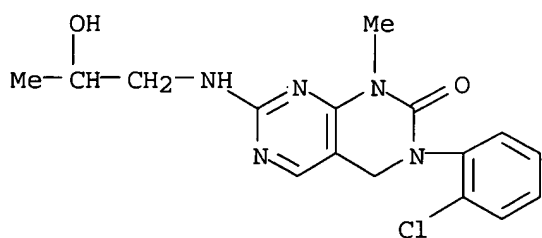
RN 335651-19-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(2-hydroxy-1-methylethyl)amino]-1-methyl- (9CI) (CA INDEX NAME)



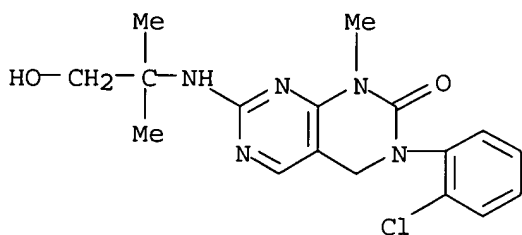
RN 335651-20-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(2-hydroxypropyl)amino]-1-methyl- (9CI) (CA INDEX NAME)



RN 335651-24-6 HCAPLUS

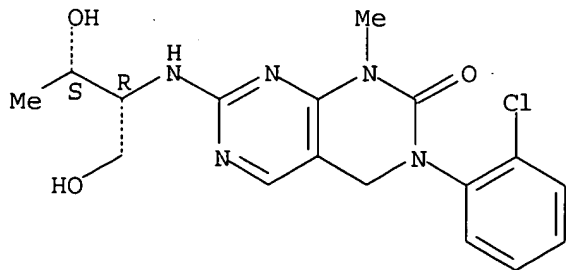
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(2-hydroxy-1,1-dimethylethyl)amino]-1-methyl- (9CI) (CA INDEX NAME)



RN 335651-30-4 HCAPLUS

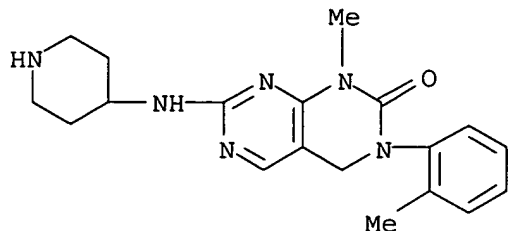
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[[(1R,2S)-2-hydroxy-1-(hydroxymethyl)propyl]amino]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



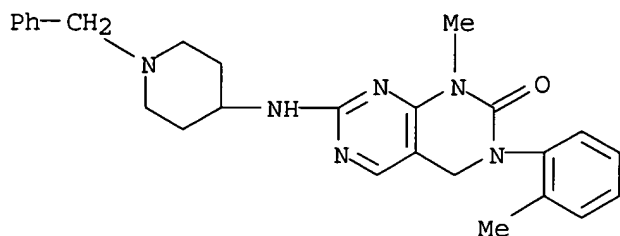
RN 335651-49-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-methyl-3-(2-methylphenyl)-7-(4-piperidinylamino)- (9CI) (CA INDEX NAME)



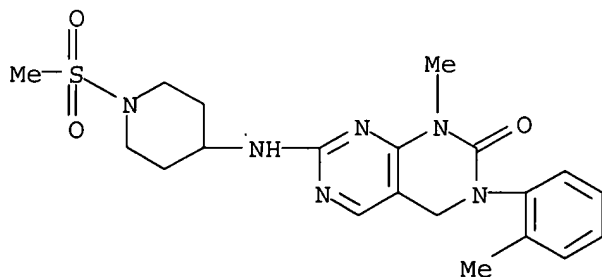
RN 335651-50-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-methyl-3-(2-methylphenyl)-7-[[1-(phenylmethyl)-4-piperidinyl]amino]- (9CI) (CA INDEX NAME)



RN 335651-53-1 HCAPLUS

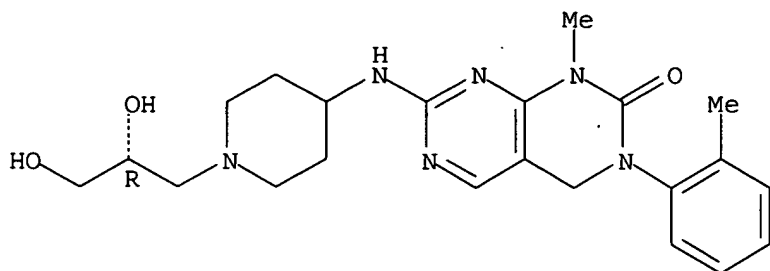
CN 4-Piperidinamine, 1-(methanesulfonyl)-N-[5,6,7,8-tetrahydro-8-methyl-6-(2-methylphenyl)-7-oxopyrimido[4,5-d]pyrimidin-2-yl]- (9CI) (CA INDEX NAME)



RN 335651-55-3 HCAPLUS

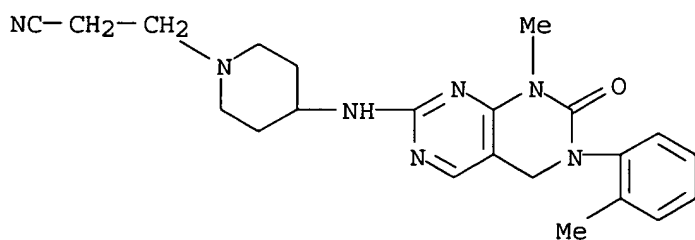
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[1-[(2R)-2,3-dihydroxypropyl]-4-piperidinyl]amino]-3,4-dihydro-1-methyl-3-(2-methylphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



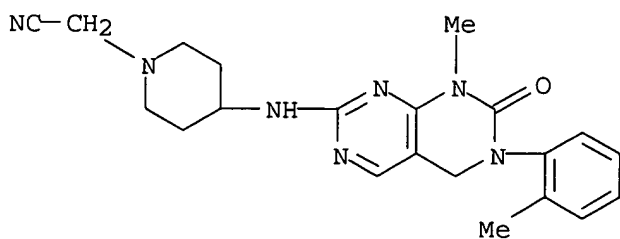
RN 335651-56-4 HCAPLUS

CN 1-Piperidinepropanenitrile, 4-[[5,6,7,8-tetrahydro-8-methyl-6-(2-methylphenyl)-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]- (9CI) (CA INDEX NAME)



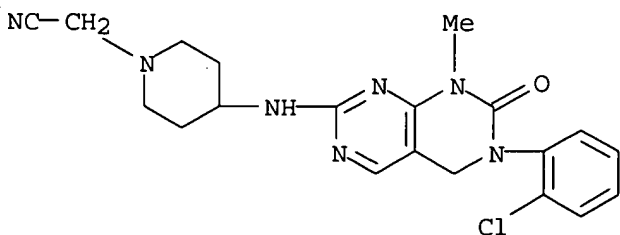
RN 335651-57-5 HCAPLUS

CN 1-Piperidineacetonitrile, 4-[[5,6,7,8-tetrahydro-8-methyl-6-(2-methylphenyl)-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]- (9CI) (CA INDEX NAME)



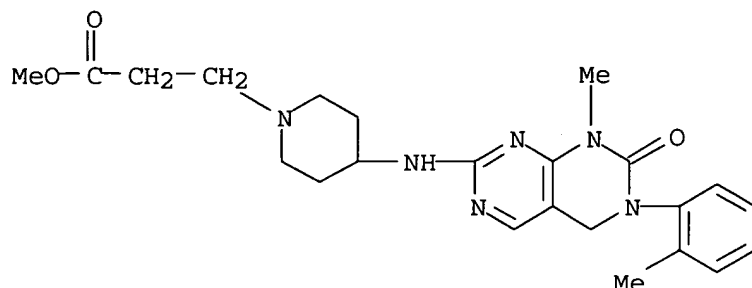
RN 335651-58-6 HCAPLUS

CN 1-Piperidineacetonitrile, 4-[[6-(2-chlorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]- (9CI) (CA INDEX NAME)



RN 335651-61-1 HCAPLUS

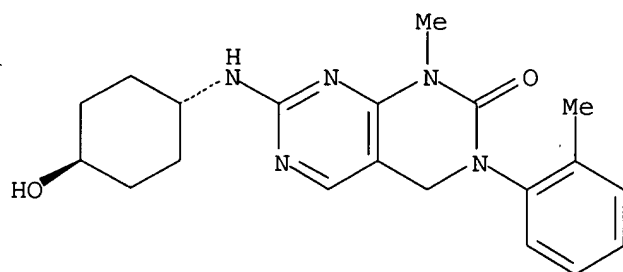
CN 1-Piperidinepropanoic acid, 4-[[5,6,7,8-tetrahydro-8-methyl-6-(2-methylphenyl)-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-, methyl ester
(9CI) (CA INDEX NAME)



RN 335651-77-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-1-methyl-3-(2-methylphenyl)- (9CI) (CA INDEX NAME)

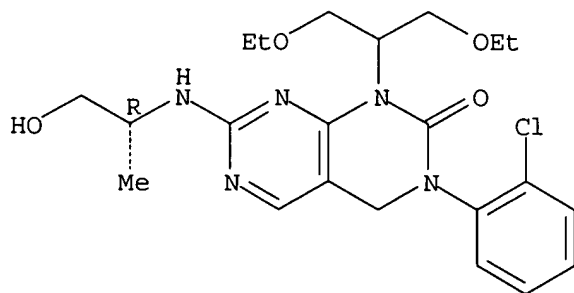
Relative stereochemistry..



RN 335651-88-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-1-[2-ethoxy-1-(ethoxymethyl)ethyl]-3,4-dihydro-7-[[(1R)-2-hydroxy-1-methylethyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

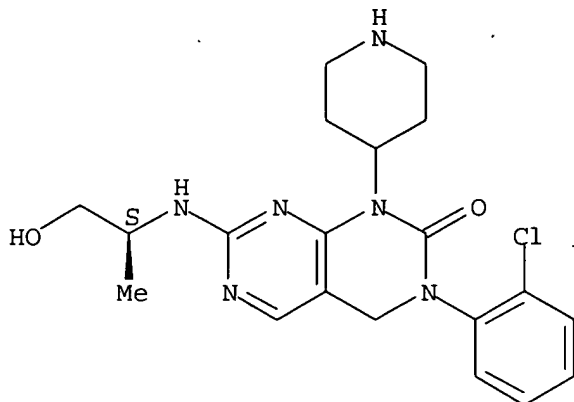


RN 335651-89-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-

[[(1S) -2-hydroxy-1-methylethyl]amino] -1- (4-piperidinyl) - (9CI) (CA INDEX NAME)

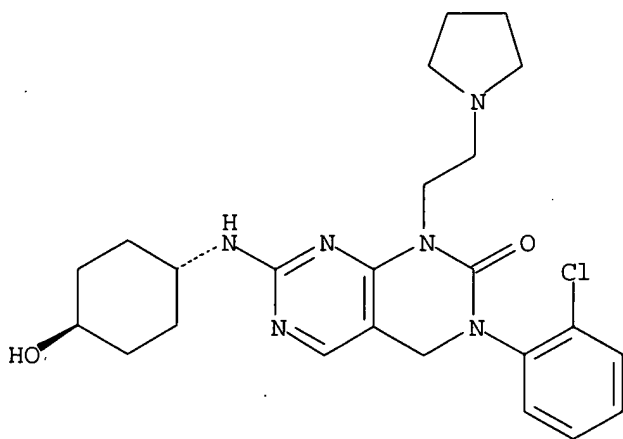
Absolute stereochemistry.



RN 335651-93-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-1-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

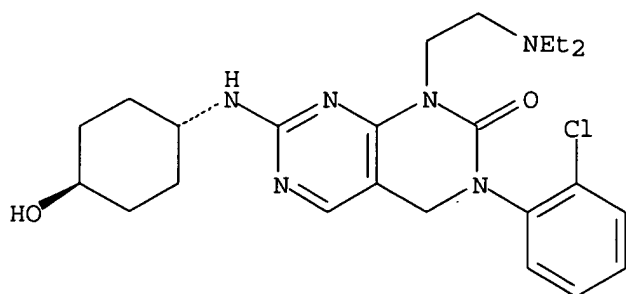
Relative stereochemistry.



RN 335651-94-0 HCAPLUS

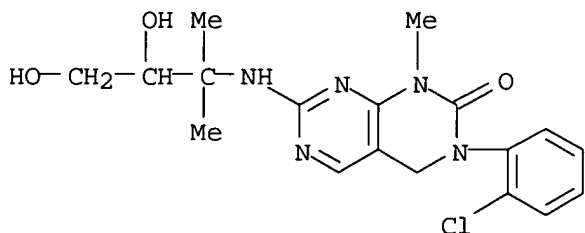
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-1-[2-(diethylamino)ethyl]-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 335651-95-1 HCAPLUS

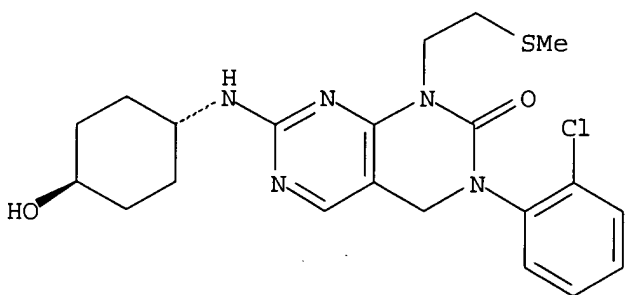
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-7-[(2,3-dihydroxy-1,1-dimethylpropyl)amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 335651-96-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-1-[2-(methylthio)ethyl]- (9CI) (CA INDEX NAME)

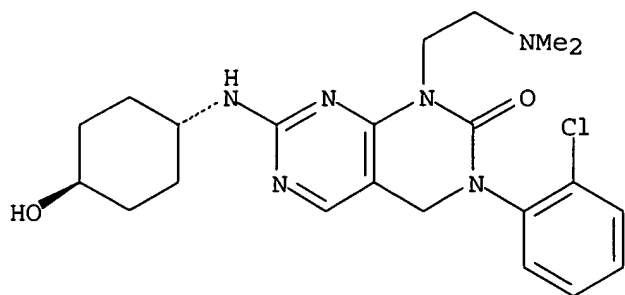
Relative stereochemistry.



RN 335651-97-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-1-[2-(dimethylamino)ethyl]-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]- (9CI) (CA INDEX NAME)

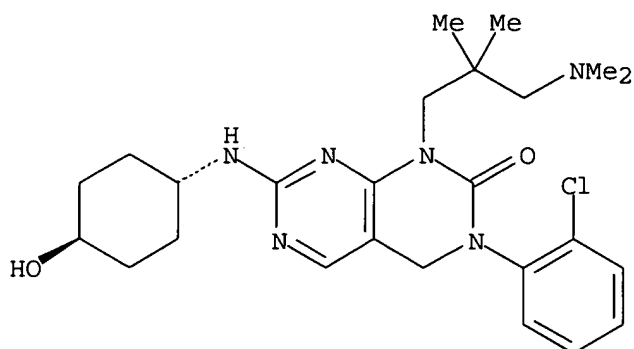
Relative stereochemistry.



RN 335651-98-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-1-[3-(dimethylamino)-2,2-dimethylpropyl]-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]- (9CI) (CA INDEX NAME)

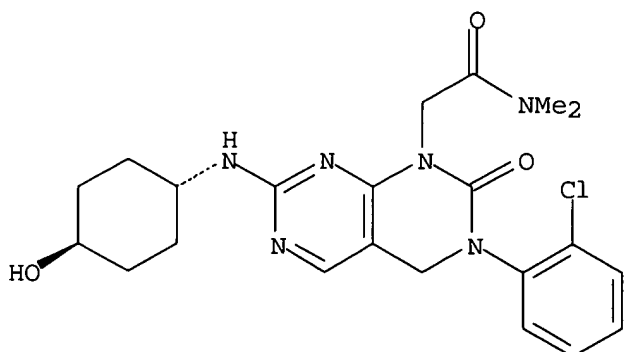
Relative stereochemistry.



RN 335651-99-5 HCAPLUS

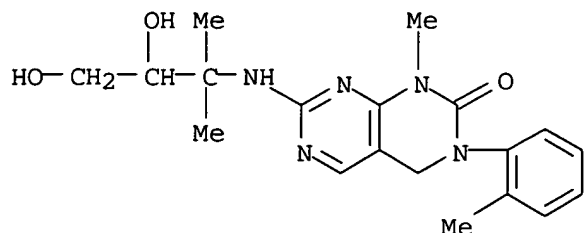
CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetamide, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-N,N-dimethyl-2-oxo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 335652-00-1 HCAPLUS

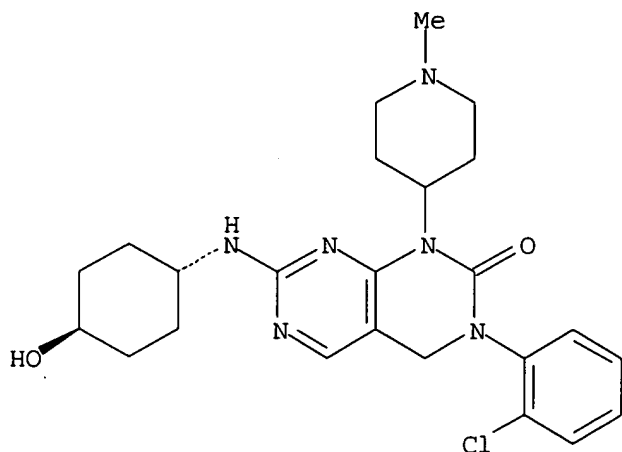
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(2,3-dihydroxy-1,1-dimethylpropyl)amino]-3,4-dihydro-1-methyl-3-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 335652-06-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-
[(trans-4-hydroxycyclohexyl)amino]-1-(1-methyl-4-piperidinyl)- (9CI) (CA
INDEX NAME)

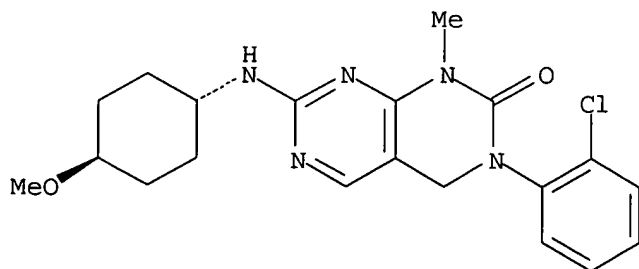
Relative stereochemistry.



RN 335652-11-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-
[(trans-4-methoxycyclohexyl)amino]-1-methyl- (9CI) (CA INDEX NAME)

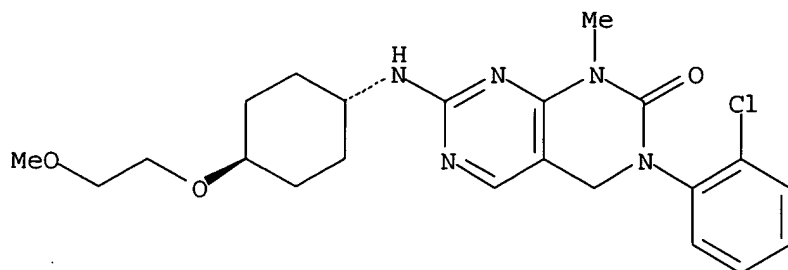
Relative stereochemistry.



RN 335652-12-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-
[[trans-4-(2-methoxyethoxy)cyclohexyl]amino]-1-methyl- (9CI) (CA INDEX
NAME)

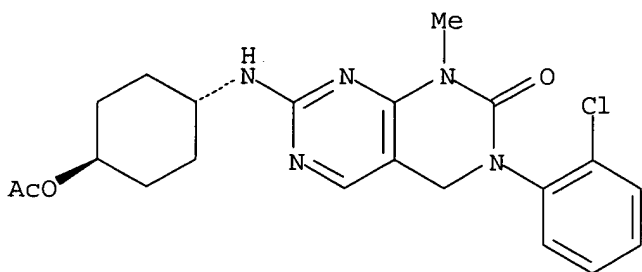
Relative stereochemistry.



RN 335652-13-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[trans-4-(acetyloxy)cyclohexyl]amino]-3-(2-chlorophenyl)-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)

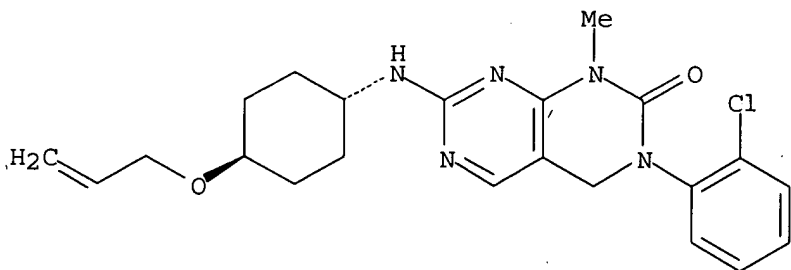
Relative stereochemistry.



RN 335652-14-7 HCAPLUS

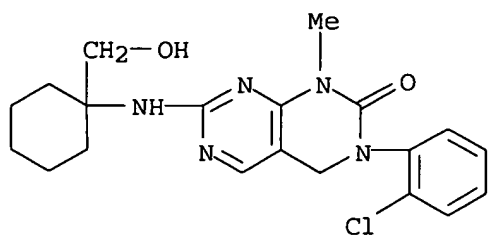
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-1-methyl-7-[[trans-4-(2-propenyloxy)cyclohexyl]amino]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 335652-16-9 HCAPLUS

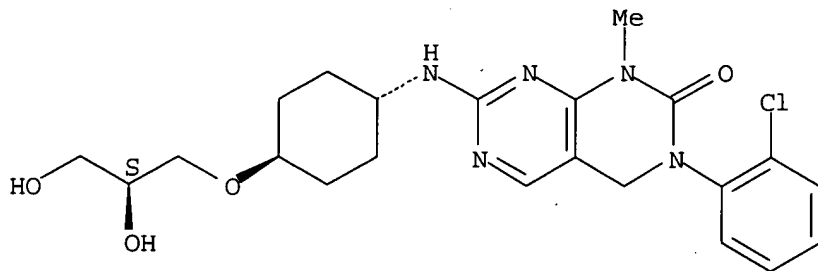
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[1-(hydroxymethyl)cyclohexyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



RN 335652-18-1 HCAPLUS

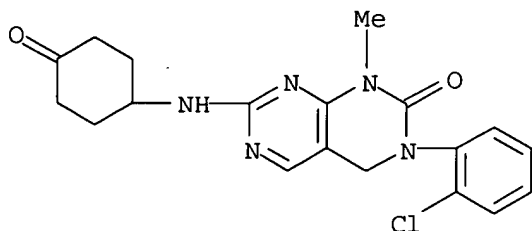
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-7-[[trans-4-[(2S)-2,3-dihydroxypropoxy]cyclohexyl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



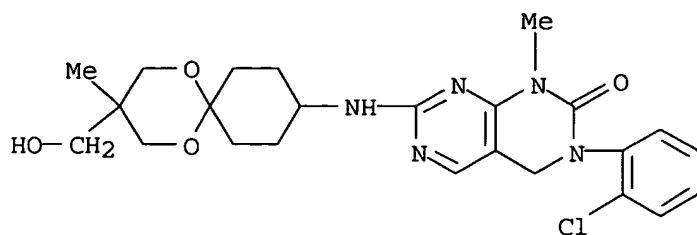
RN 335652-22-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-1-methyl-7-[(4-oxocyclohexyl)amino]- (9CI) (CA INDEX NAME)



RN 335652-24-9 HCAPLUS

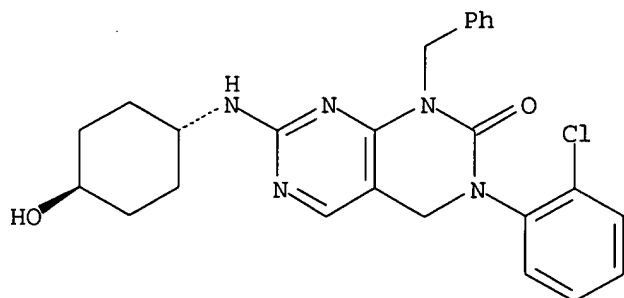
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[3-(hydroxymethyl)-3-methyl-1,5-dioxaspiro[5.5]undec-9-yl]amino]-1-methyl- (9CI) (CA INDEX NAME)



RN 335652-26-1 HCAPLUS

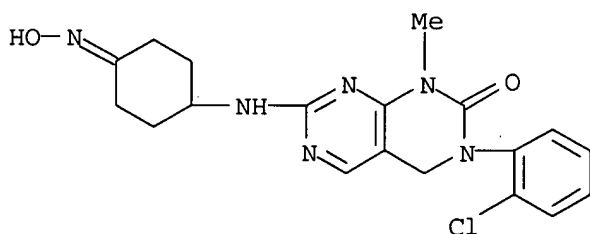
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-1-(phenylmethyl)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 335652-30-7 HCAPLUS

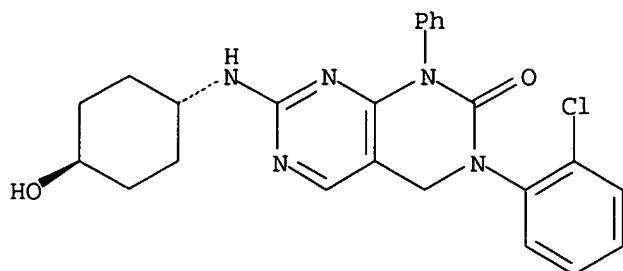
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[4-(hydroxyimino)cyclohexyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



RN 335652-32-9 HCAPLUS

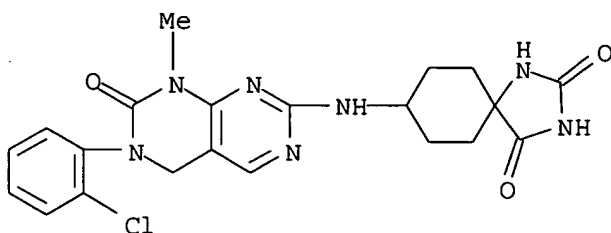
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-1-phenyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 335652-36-3 HCAPLUS

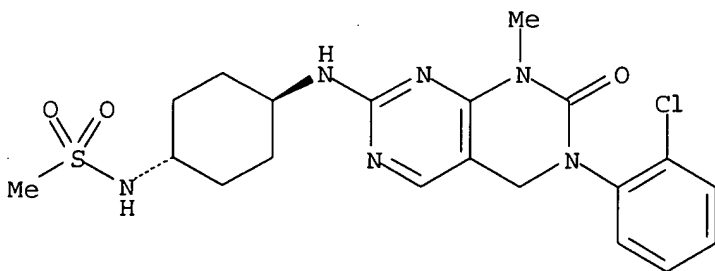
CN 1,3-Diazaspiro[4.5]decane-2,4-dione, 8-[[6-(2-chlorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]- (9CI) (CA INDEX NAME)



RN 335652-39-6 HCAPLUS

CN Methanesulfonamide, N-[trans-4-[[6-(2-chlorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]cyclohexyl]- (9CI) (CA INDEX NAME)

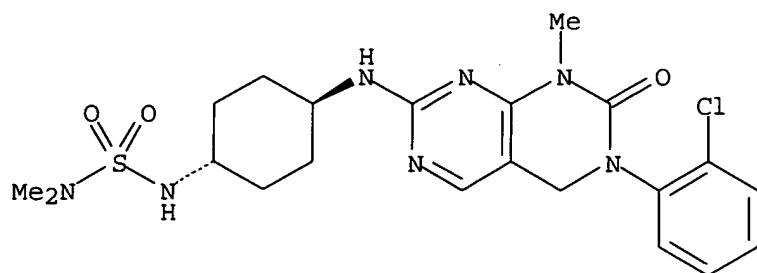
Relative stereochemistry.



RN 335652-40-9 HCAPLUS

CN Sulfamide, N'-[trans-4-[[6-(2-chlorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]cyclohexyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

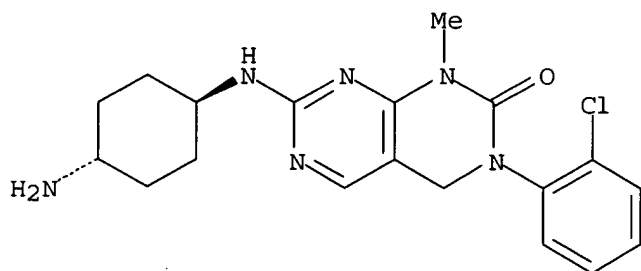
Relative stereochemistry.



RN 335652-41-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(trans-4-aminocyclohexyl)amino]-3-(2-chlorophenyl)-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 335651-18-8P 335651-21-3P 335651-22-4P
 335651-23-5P 335651-25-7P 335651-26-8P
 335651-27-9P 335651-28-0P 335651-29-1P
 335651-31-5P 335651-32-6P 335651-33-7P
 335651-34-8P 335651-36-0P 335651-37-1P
 335651-38-2P 335651-39-3P 335651-40-6P
 335651-41-7P 335651-42-8P 335651-43-9P
 335651-44-0P 335651-45-1P 335651-46-2P
 335651-47-3P 335651-48-4P 335651-52-0P
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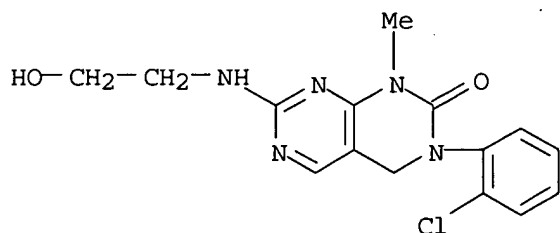
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 335653-37-7P 335653-38-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of alkylamino substituted pyrimidino[4,5-d]pyrimidines for pharmaceutical use as inhibitors of p38 protein kinase)

RN 335651-18-8 HCAPLUS

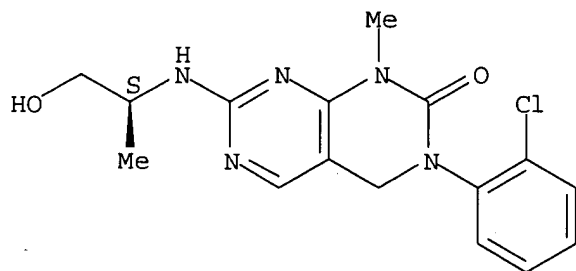
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(2-hydroxyethyl)amino]-1-methyl- (9CI) (CA INDEX NAME)



RN 335651-21-3 HCAPLUS

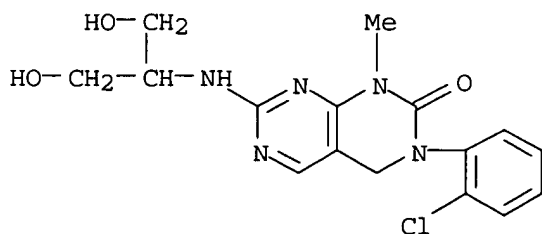
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[1S]-2-hydroxy-1-methylethyl]amino]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 335651-22-4 HCAPLUS

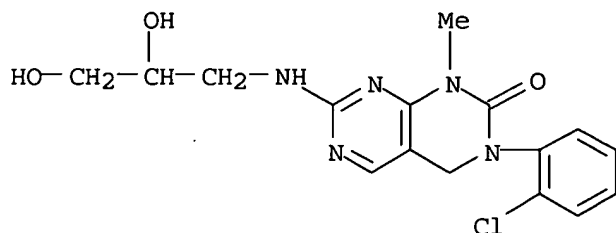
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



RN 335651-23-5 HCAPLUS

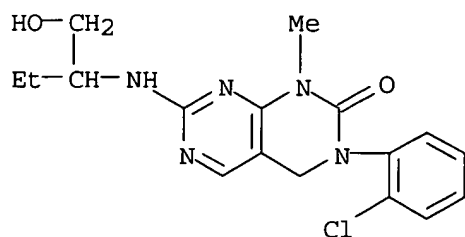
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-7-[(2,3-

dihydroxypropyl)amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



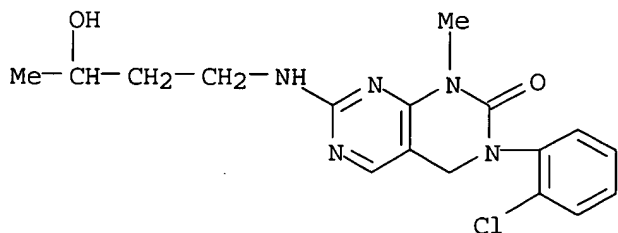
RN 335651-25-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[1-(2-hydroxypropyl)amino]-1-methyl- (9CI) (CA INDEX NAME)



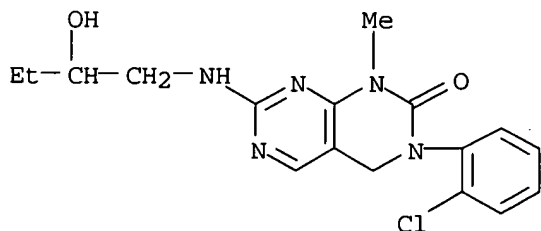
RN 335651-26-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[3-hydroxybutyl)amino]-1-methyl- (9CI) (CA INDEX NAME)



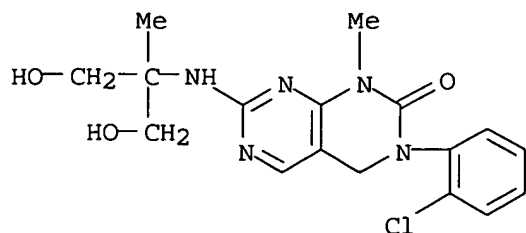
RN 335651-27-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(2-hydroxybutyl)amino]-1-methyl- (9CI) (CA INDEX NAME)



RN 335651-28-0 HCAPLUS

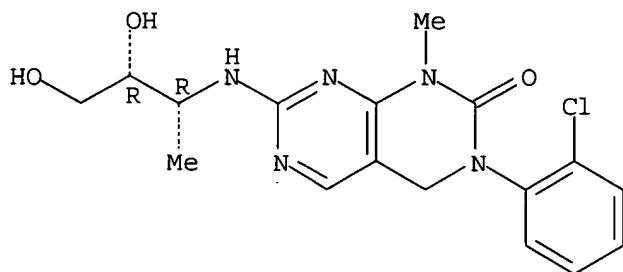
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[2-hydroxy-1-(hydroxymethyl)-1-methylethyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



RN 335651-29-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-7-[[[(1R,2R)-2,3-dihydroxy-1-methylpropyl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)

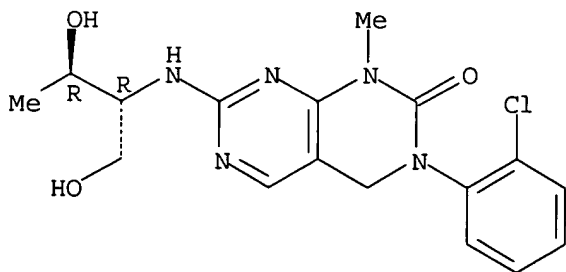
Absolute stereochemistry.



RN 335651-31-5 HCAPLUS

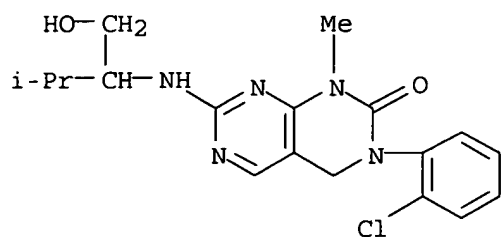
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[[(1R,2R)-2-hydroxy-1-(hydroxymethyl)propyl]amino]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



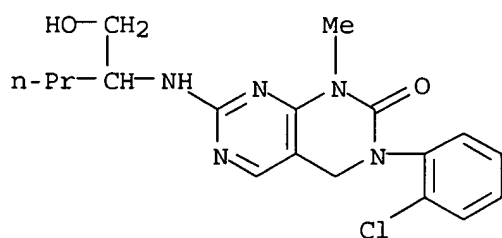
RN 335651-32-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[[1-(hydroxymethyl)-2-methylpropyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



RN 335651-33-7 HCAPLUS

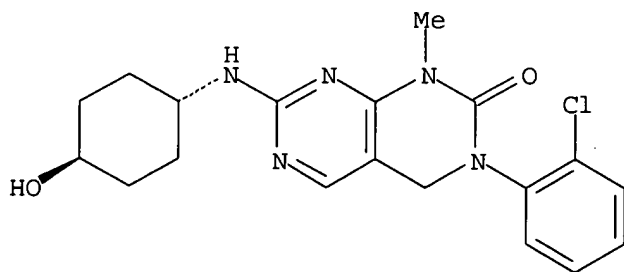
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[1-(hydroxymethyl)butyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



RN 335651-34-8 HCAPLUS

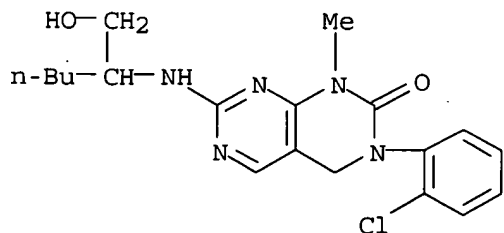
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-1-methyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 335651-36-0 HCAPLUS

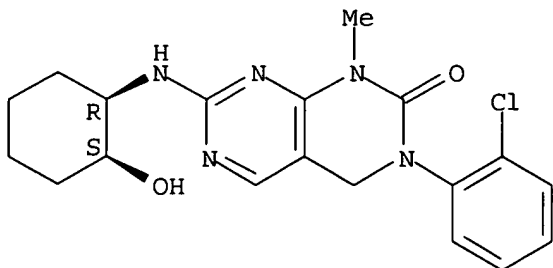
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[1-(hydroxymethyl)pentyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



RN 335651-37-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-
[[(1R,2S)-2-hydroxycyclohexyl]amino]-1-methyl-, rel- (9CI) (CA INDEX
NAME)

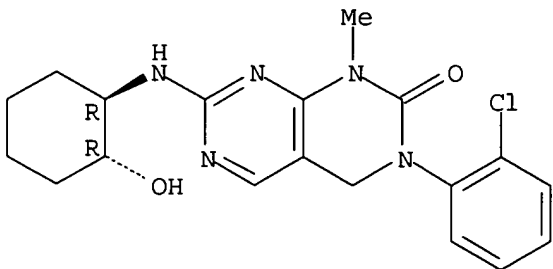
Relative stereochemistry.



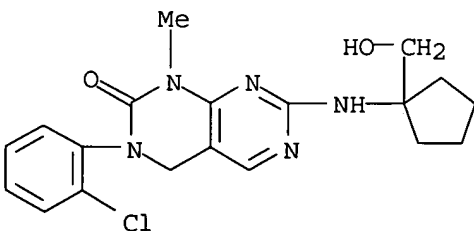
RN 335651-38-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-
[[(1R,2R)-2-hydroxycyclohexyl]amino]-1-methyl-, rel- (9CI) (CA INDEX
NAME)

Relative stereochemistry.



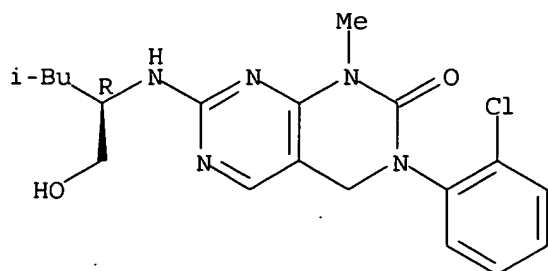
RN 335651-39-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[1-
(hydroxymethyl)cyclopentyl]amino]-1-methyl- (9CI) (CA INDEX NAME)

RN 335651-40-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-
[[(1R)-1-(hydroxymethyl)-3-methylbutyl]amino]-1-methyl- (9CI) (CA INDEX
NAME)

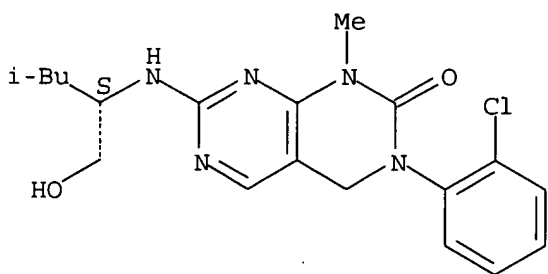
Absolute stereochemistry.



RN 335651-41-7 HCAPLUS

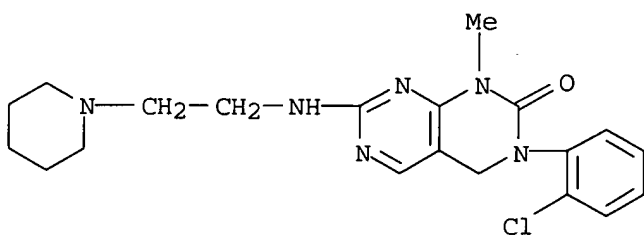
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[(1S)-1-(hydroxymethyl)-3-methylbutyl]amino]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



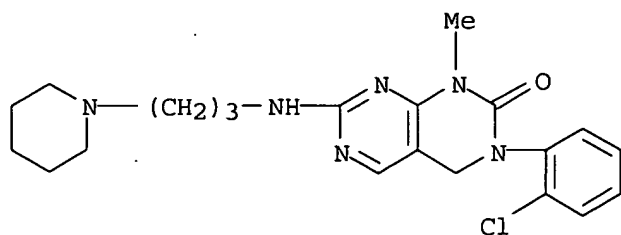
RN 335651-42-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-1-methyl-7-[[2-(1-piperidinyl)ethyl]amino]- (9CI) (CA INDEX NAME)



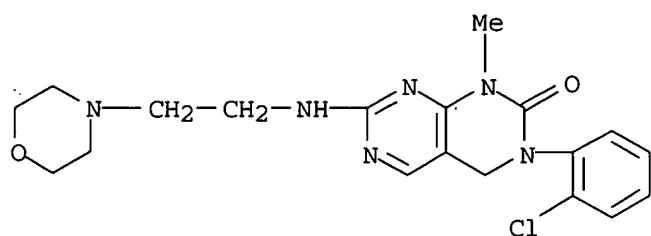
RN 335651-43-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-1-methyl-7-[[3-(1-piperidinyl)propyl]amino]- (9CI) (CA INDEX NAME)



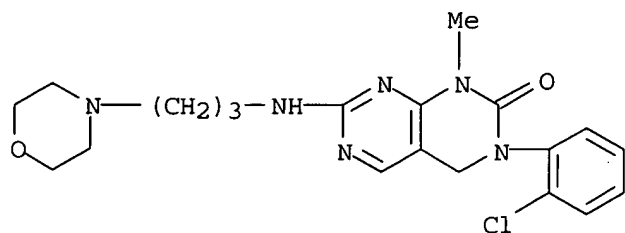
RN 335651-44-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-1-methyl-7-[[2-(4-morpholinyl)ethyl]amino] - (9CI) (CA INDEX NAME)



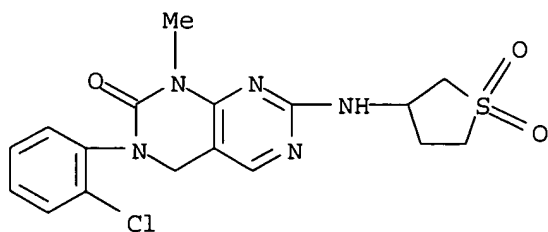
RN 335651-45-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-1-methyl-7-[[3-(4-morpholinyl)propyl]amino] - (9CI) (CA INDEX NAME)



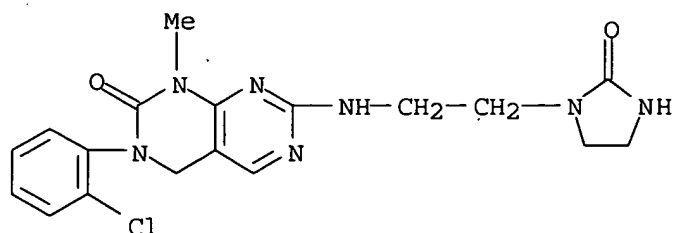
RN 335651-46-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-1-methyl-7-[(tetrahydro-1,1-dioxido-3-thienyl)amino] - (9CI) (CA INDEX NAME)



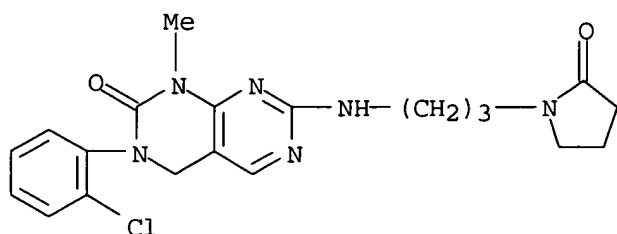
RN 335651-47-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-1-methyl-7-[[2-(2-oxo-1-imidazolidinyl)ethyl]amino] - (9CI) (CA INDEX NAME)



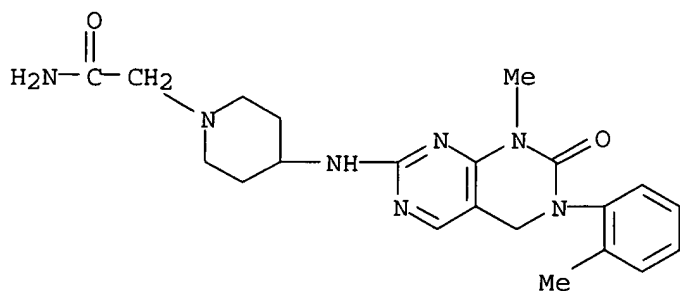
RN 335651-48-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-1-methyl-7-[[3-(2-oxo-1-pyrrolidinyl)propyl]amino] - (9CI) (CA INDEX NAME)



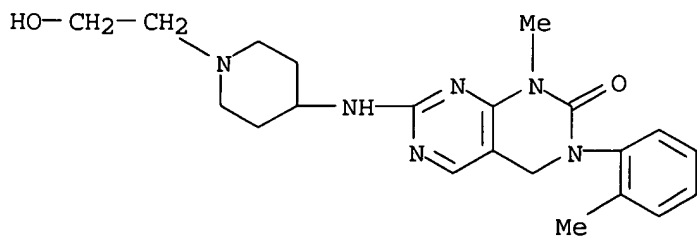
RN 335651-52-0 HCAPLUS

CN 1-Piperidineacetamide, 4-[[5,6,7,8-tetrahydro-8-methyl-6-(2-methylphenyl)-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino] - (9CI) (CA INDEX NAME)



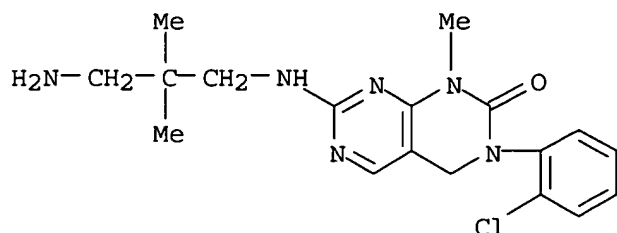
RN 335651-54-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-7-[[1-(2-hydroxyethyl)-4-piperidinyl]amino]-1-methyl-3-(2-methylphenyl) - (9CI) (CA INDEX NAME)



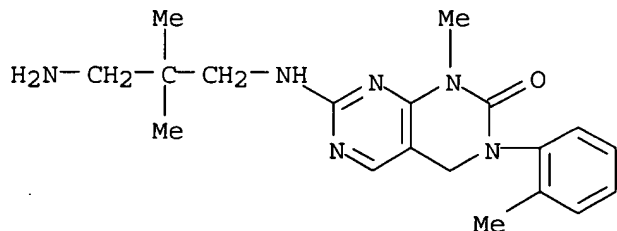
RN 335651-70-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(3-amino-2,2-dimethylpropyl)amino]-3-(2-chlorophenyl)-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



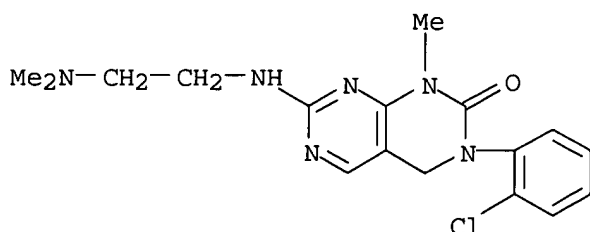
RN 335651-71-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(3-amino-2,2-dimethylpropyl)amino]-3,4-dihydro-1-methyl-3-(2-methylphenyl)- (9CI) (CA INDEX NAME)



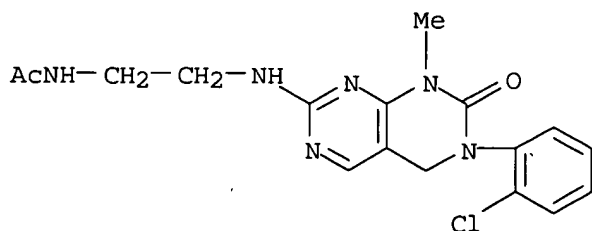
RN 335651-72-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-7-[[2-(dimethylamino)ethyl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



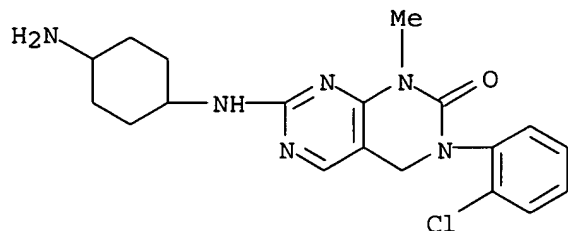
RN 335651-73-5 HCAPLUS

CN Acetamide, N-[2-[[6-(2-chlorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]ethyl]- (9CI) (CA INDEX NAME)



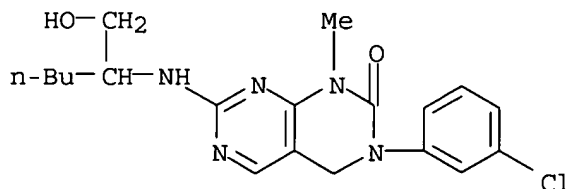
RN 335651-74-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(4-aminocyclohexyl)amino]-3-(2-chlorophenyl)-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



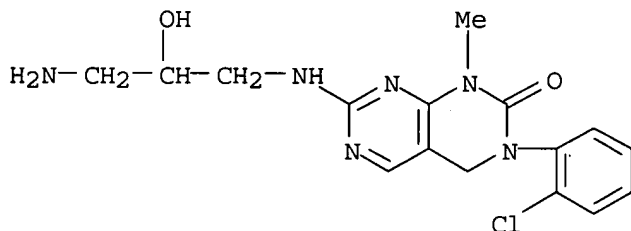
RN 335651-75-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(3-chlorophenyl)-3,4-dihydro-7-[[1-(hydroxymethyl)pentyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



RN 335651-76-8 HCAPLUS

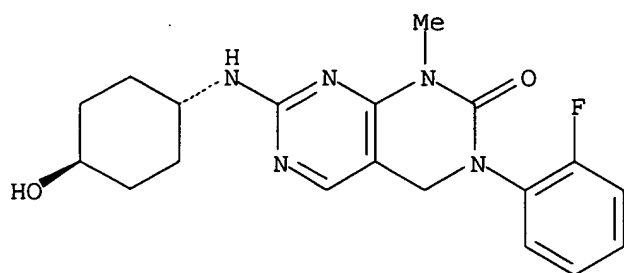
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(3-amino-2-hydroxypropyl)amino]-3-(2-chlorophenyl)-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 335651-78-0 HCAPLUS

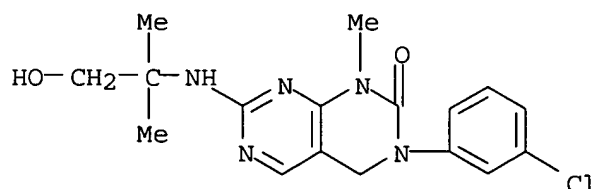
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-fluorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-1-methyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.



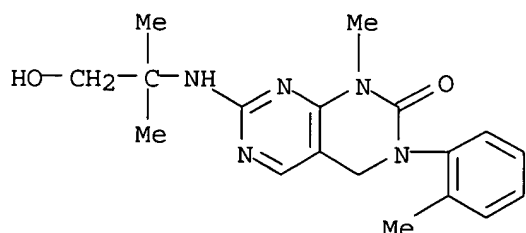
RN 335651-79-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(3-chlorophenyl)-3,4-dihydro-7-[(2-hydroxy-1,1-dimethylethyl)amino]-1-methyl- (9CI) (CA INDEX NAME)



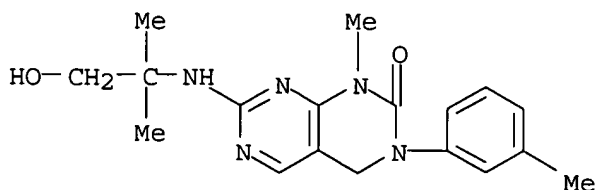
RN 335651-80-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-7-[(2-hydroxy-1,1-dimethylethyl)amino]-1-methyl-3-(2-methylphenyl)- (9CI) (CA INDEX NAME)



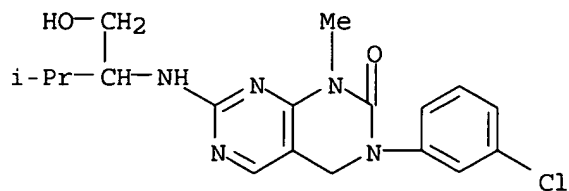
RN 335651-81-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-7-[(2-hydroxy-1,1-dimethylethyl)amino]-1-methyl-3-(3-methylphenyl)- (9CI) (CA INDEX NAME)



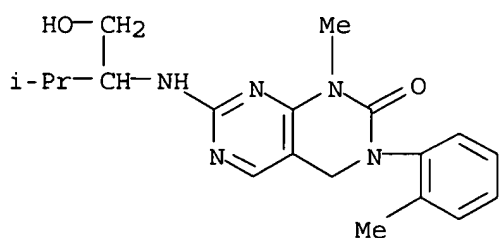
RN 335651-82-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(3-chlorophenyl)-3,4-dihydro-7-[[1-(hydroxymethyl)-2-methylpropyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



RN 335651-83-7 HCAPLUS

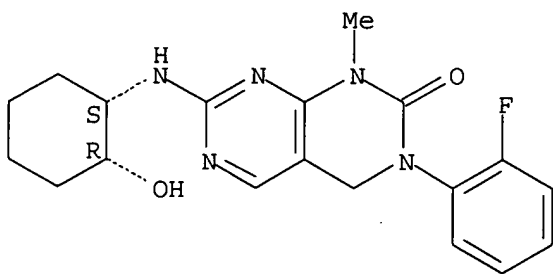
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-7-[[1-(hydroxymethyl)-2-methylpropyl]amino]-1-methyl-3-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 335651-84-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-fluorophenyl)-3,4-dihydro-7-[[1-(1R,2S)-2-hydroxycyclohexyl]amino]-1-methyl-, rel- (9CI) (CA INDEX NAME)

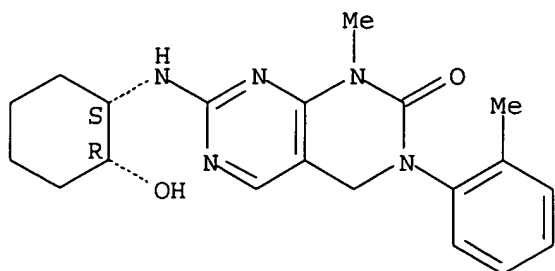
Relative stereochemistry.



RN 335651-85-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-methylphenyl)-3,4-dihydro-7-[[1-(1R,2S)-2-hydroxycyclohexyl]amino]-1-methyl-, rel- (9CI) (CA INDEX NAME)

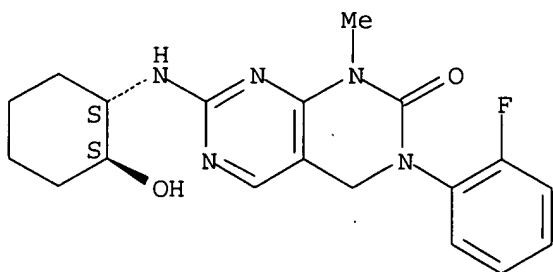
Relative stereochemistry.



RN 335651-86-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-fluorophenyl)-3,4-dihydro-7-[[(1R,2R) -2-hydroxycyclohexyl]amino]-1-methyl-, rel- (9CI) (CA INDEX NAME)

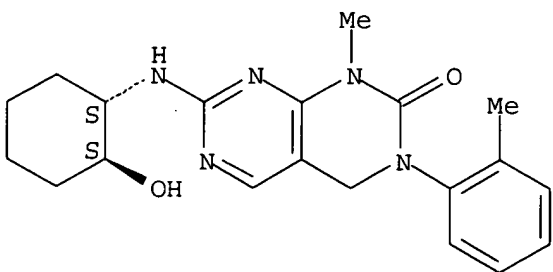
Relative stereochemistry.



RN 335651-87-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-7-[[(1R,2R) -2-hydroxycyclohexyl]amino]-1-methyl-3-(2-methylphenyl)-, rel- (9CI) (CA INDEX NAME)

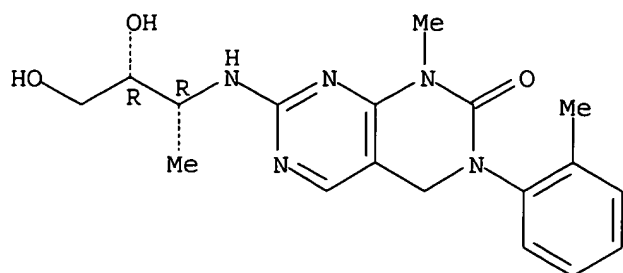
Relative stereochemistry.



RN 335651-90-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[(1R,2R) -2,3-dihydroxy-1-methylpropyl]amino]-3,4-dihydro-1-methyl-3-(2-methylphenyl)- (9CI) (CA INDEX NAME)

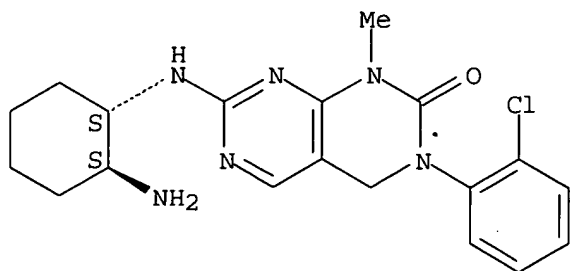
Absolute stereochemistry.



RN 335651-91-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[[(1S,2S)-2-aminocyclohexyl]amino]-3-(2-chlorophenyl)-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)

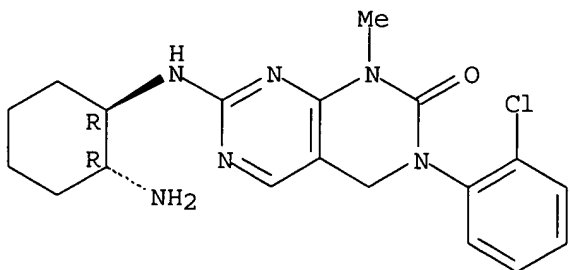
Absolute stereochemistry.



RN 335651-92-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[[(1R,2R)-2-aminocyclohexyl]amino]-3-(2-chlorophenyl)-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)

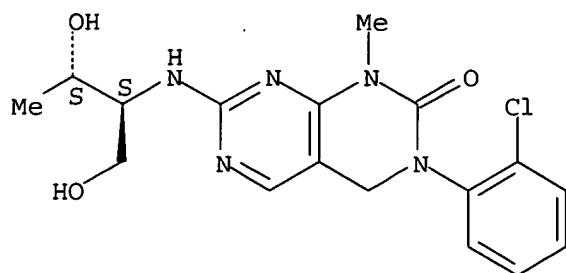
Absolute stereochemistry.



RN 335652-02-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[[(1S,2S)-2-hydroxy-1-(hydroxymethyl)propyl]amino]-1-methyl- (9CI) (CA INDEX NAME)

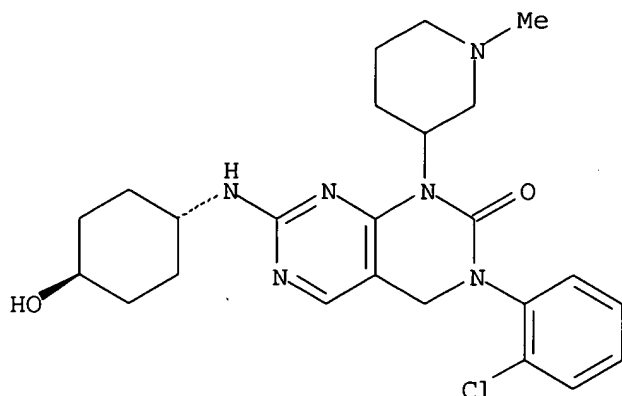
Absolute stereochemistry.



RN 335652-04-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-1-(1-methyl-3-piperidinyl)- (9CI) (CA INDEX NAME)

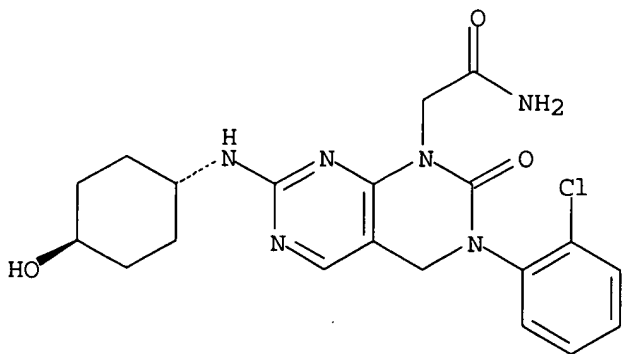
Relative stereochemistry.



RN 335652-08-9 HCAPLUS

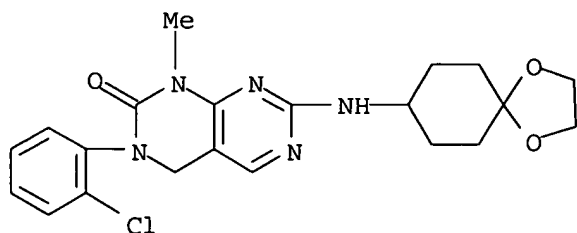
CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetamide, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-2-oxo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 335652-20-5 HCAPLUS

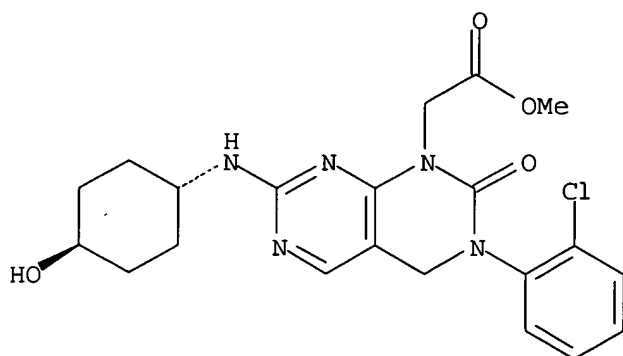
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-7-(1,4-dioxaspiro[4.5]dec-8-ylamino)-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 335652-28-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetic acid, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-2-oxo-, methyl ester (9CI) (CA INDEX NAME)

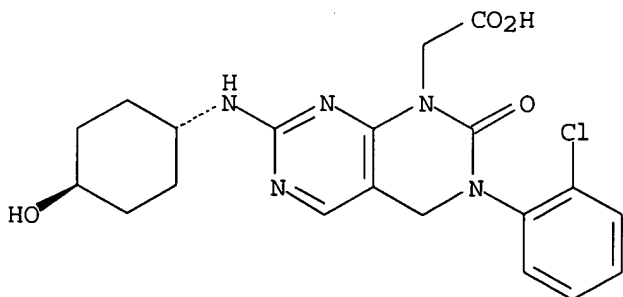
Relative stereochemistry.



RN 335652-34-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetic acid, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-2-oxo- (9CI) (CA INDEX NAME)

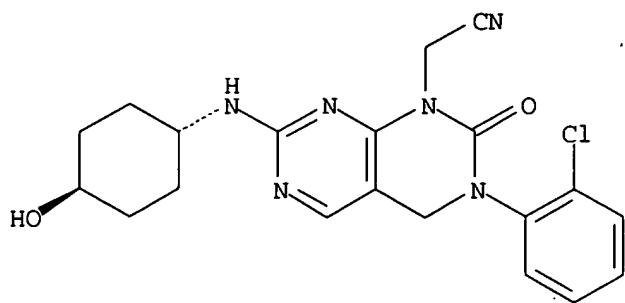
Relative stereochemistry.



RN 335652-37-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetonitrile, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-2-oxo- (9CI) (CA INDEX NAME)

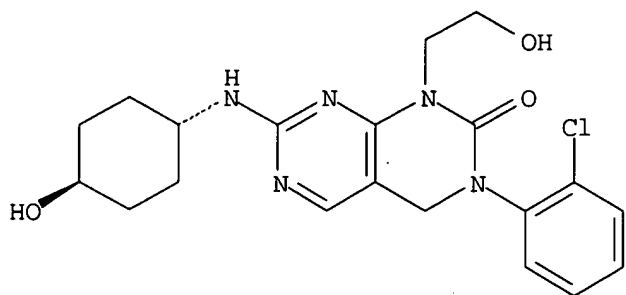
Relative stereochemistry.



RN 335652-38-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-1-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

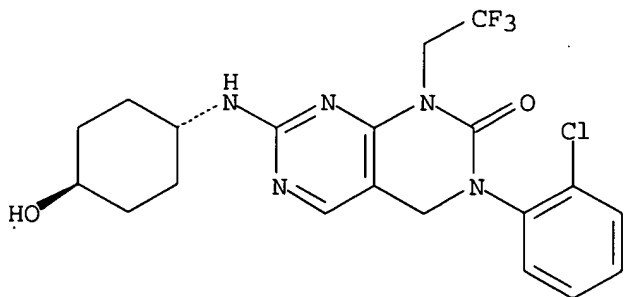
Relative stereochemistry.



RN 335652-42-1 HCAPLUS

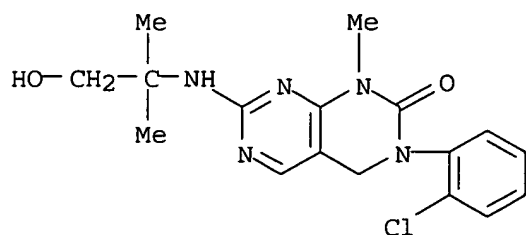
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-1-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 335652-71-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(2-hydroxy-1,1-dimethylethyl)amino]-1-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

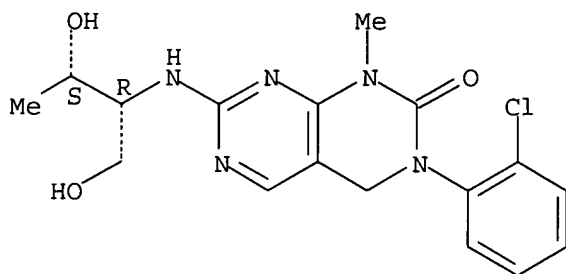


● HCl

RN 335652-72-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[(1R,2S)-2-hydroxy-1-(hydroxymethyl)propyl]amino]-1-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

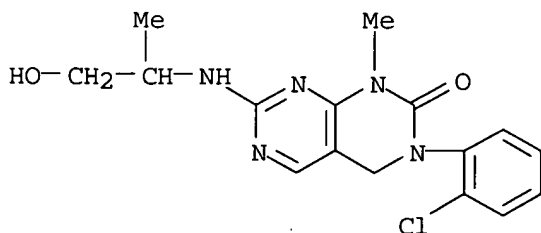
Absolute stereochemistry.



● HCl

RN 335652-73-8 HCAPLUS

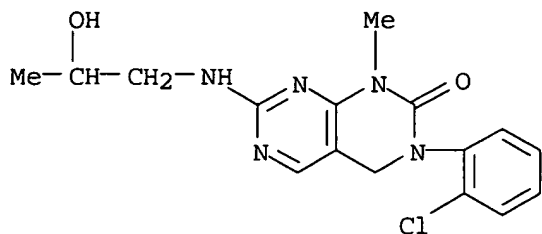
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(2-hydroxy-1-methylethyl)amino]-1-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 335652-74-9 HCAPLUS

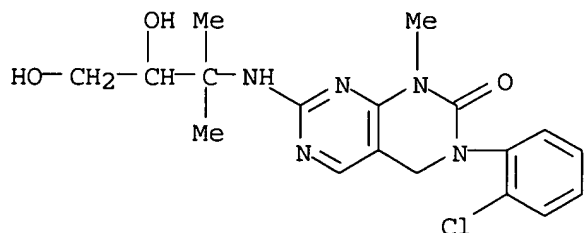
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(2-hydroxypropyl)amino]-1-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 335652-75-0 HCAPLUS

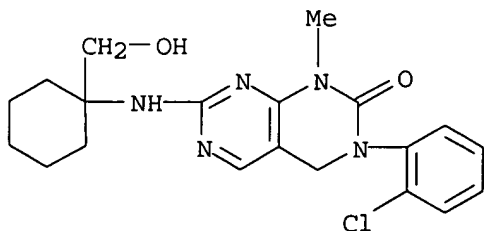
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-7-[(2,3-dihydroxy-1,1-dimethylpropyl)amino]-3,4-dihydro-1-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 335652-76-1 HCAPLUS

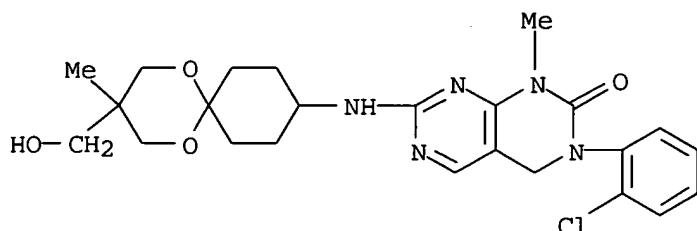
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[1-(hydroxymethyl)cyclohexyl]amino]-1-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 335652-77-2 HCAPLUS

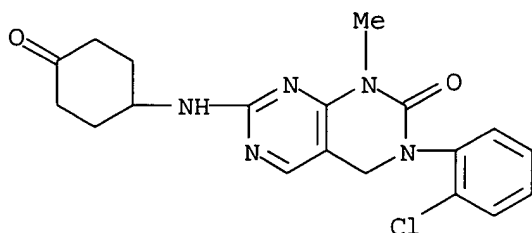
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[3-(hydroxymethyl)-3-methyl-1,5-dioxaspiro[5.5]undec-9-yl]amino]-1-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 335652-78-3 HCAPLUS

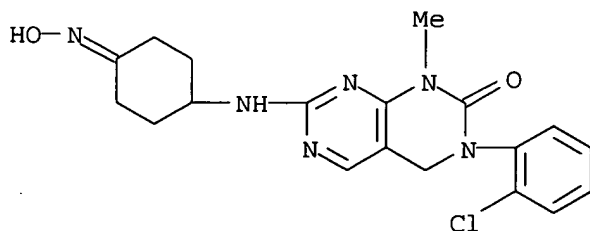
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-1-methyl-7-[(4-oxocyclohexyl)amino]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 335652-79-4 HCAPLUS

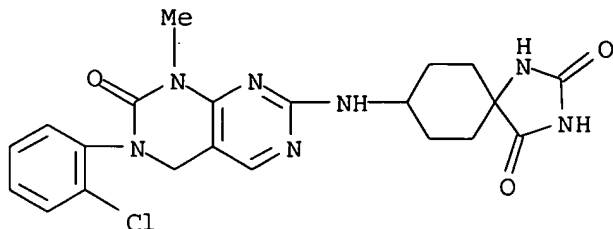
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[[4-(hydroxyimino)cyclohexyl]amino]-1-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 335652-80-7 HCAPLUS

CN 1,3-Diazaspiro[4.5]decane-2,4-dione, 8-[[6-(2-chlorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

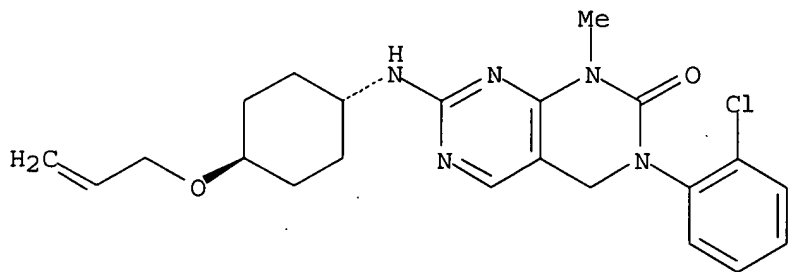


● HCl

RN 335652-81-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-1-methyl-7-[[trans-4-(2-propenyloxy)cyclohexyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

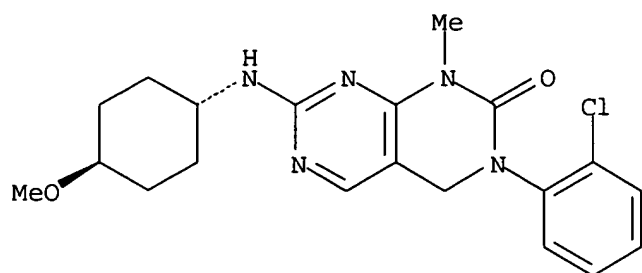


● HCl

RN 335652-82-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-methoxycyclohexyl)amino]-1-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

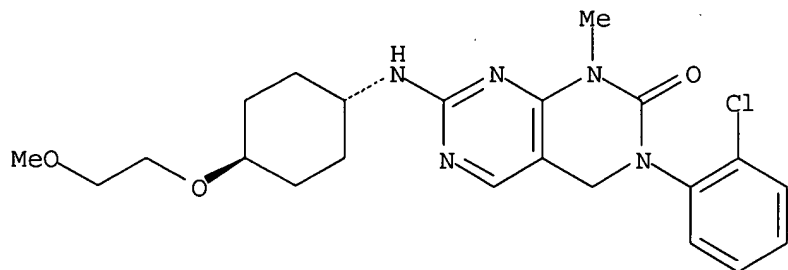
Relative stereochemistry.



● HCl

RN 335652-83-0 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-
 [[trans-4-(2-methoxyethoxy)cyclohexyl]amino]-1-methyl-, monohydrochloride
 (9CI) (CA INDEX NAME)

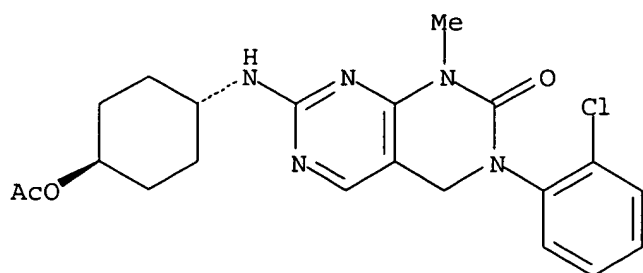
Relative stereochemistry.



● HCl

RN 335652-84-1 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[trans-4-(
 (acetyloxy)cyclohexyl]amino)-3-(2-chlorophenyl)-3,4-dihydro-1-methyl-,
 monohydrochloride (9CI) (CA INDEX NAME)

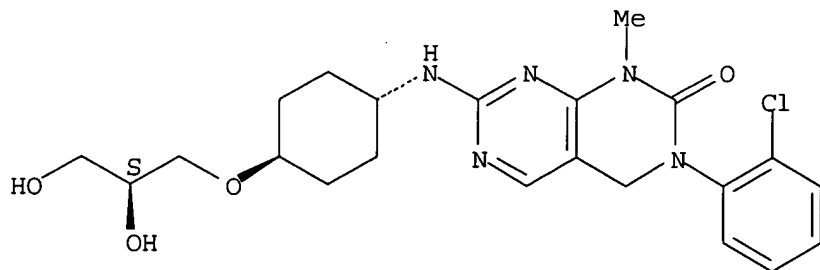
Relative stereochemistry.



● HCl

RN 335652-85-2 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-7-[[trans-4-[(2S)-2,3-dihydroxypropoxy]cyclohexyl]amino]-3,4-dihydro-1-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

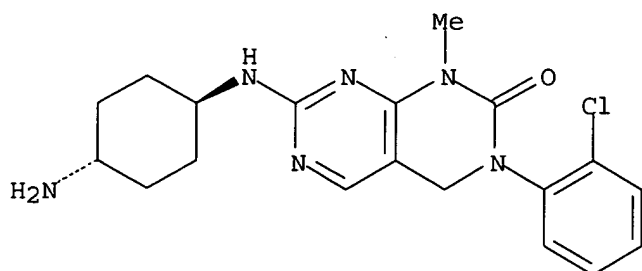
Absolute stereochemistry.



● HCl

RN 335652-86-3 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(trans-4-aminocyclohexyl)amino]-3-(2-chlorophenyl)-3,4-dihydro-1-methyl-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

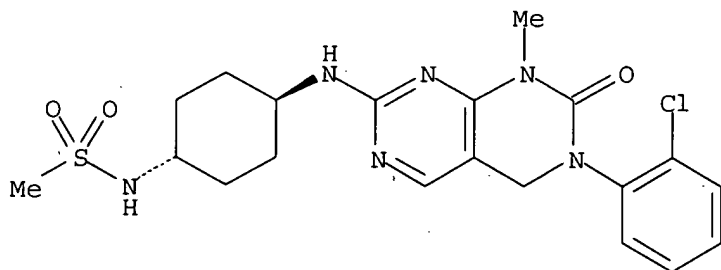


● 2 HCl

RN 335652-87-4 HCAPLUS

CN Methanesulfonamide, N-[trans-4-[[6-(2-chlorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]cyclohexyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

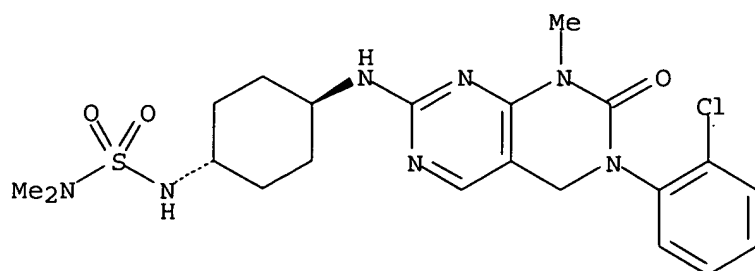


● HCl

RN 335652-88-5 HCAPLUS

CN Sulfamide, N'-[trans-4-[[6-(2-chlorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]cyclohexyl]-N,N-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)

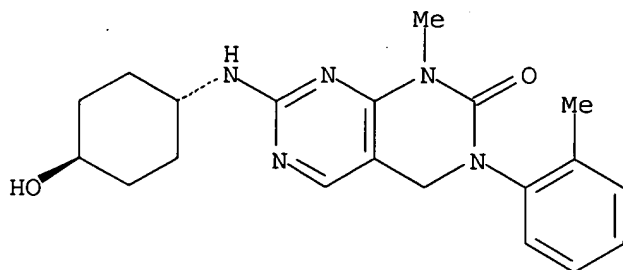
Relative stereochemistry.



● HCl

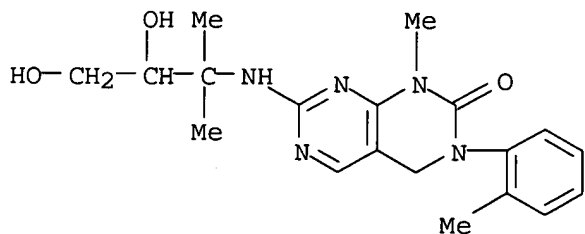
RN 335652-90-9 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-1-methyl-3-(2-methylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

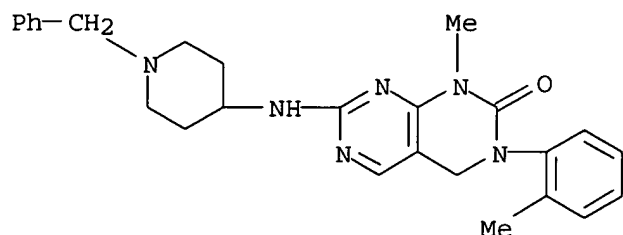
RN 335652-91-0 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(2,3-dihydroxy-1,1-dimethylpropyl)amino]-3,4-dihydro-1-methyl-3-(2-methylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 335652-92-1 HCAPLUS

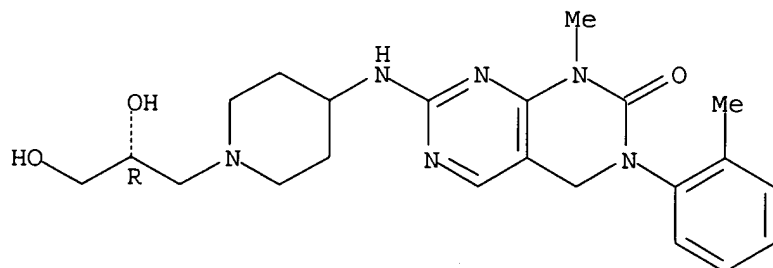
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-1-methyl-3-(2-methylphenyl)-7-[[1-(phenylmethyl)-4-piperidinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 335652-93-2 HCAPLUS

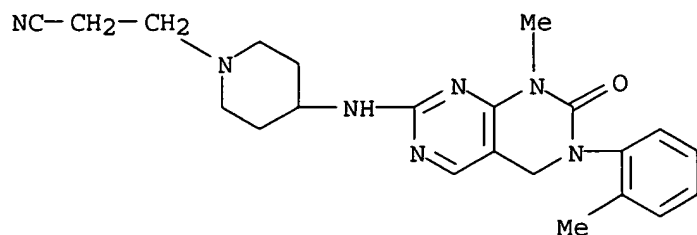
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[1-[(2R)-2,3-dihydroxypropyl]-4-piperidinyl]amino]-3,4-dihydro-1-methyl-3-(2-methylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 335652-94-3 HCAPLUS

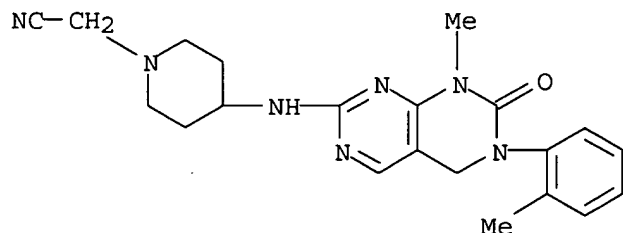
CN 1-Piperidinepropanenitrile, 4-[[5,6,7,8-tetrahydro-8-methyl-6-(2-methylphenyl)-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 335652-95-4 HCAPLUS

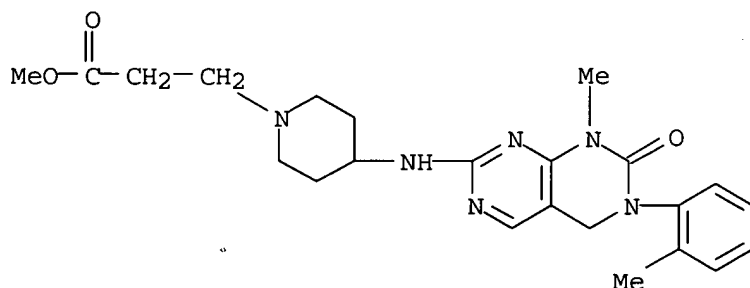
CN 1-Piperidineacetonitrile, 4-[[5,6,7,8-tetrahydro-8-methyl-6-(2-methylphenyl)-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 335652-96-5 HCAPLUS

CN 1-Piperidinepropanoic acid, 4-[[5,6,7,8-tetrahydro-8-methyl-6-(2-methylphenyl)-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

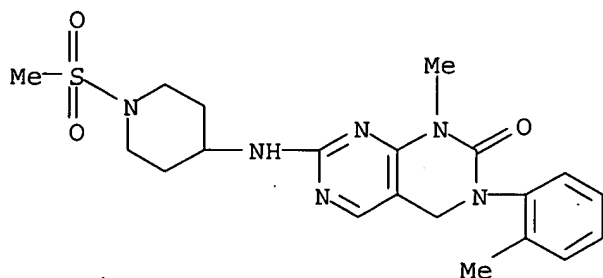


● HCl

RN 335652-98-7 HCAPLUS

CN 4-Piperidinamine, 1-(methanesulfonyl)-N-[5,6,7,8-tetrahydro-8-methyl-6-(2-

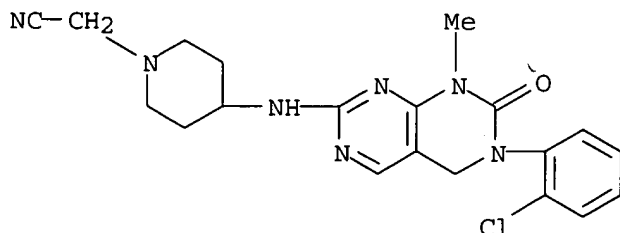
methylphenyl)-7-oxopyrimido[4,5-d]pyrimidin-2-yl]-, monohydrochloride
(9CI) (CA INDEX NAME)



● HCl

RN 335652-99-8 HCAPLUS

CN 1-Piperidineacetonitrile, 4-[[6-(2-chlorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-, monohydrochloride (9CI)
(CA INDEX NAME)

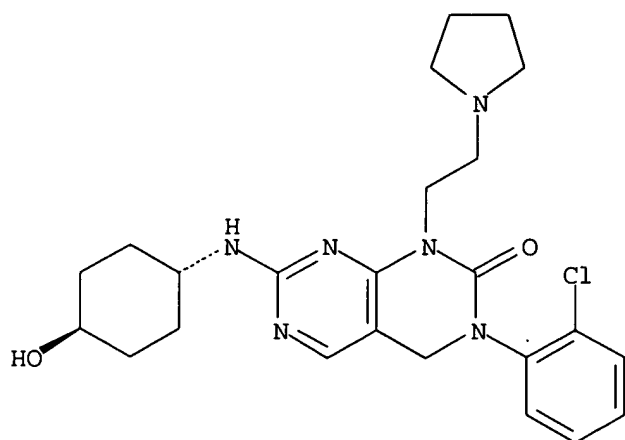


● HCl

RN 335653-00-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-1-[2-(1-pyrrolidinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

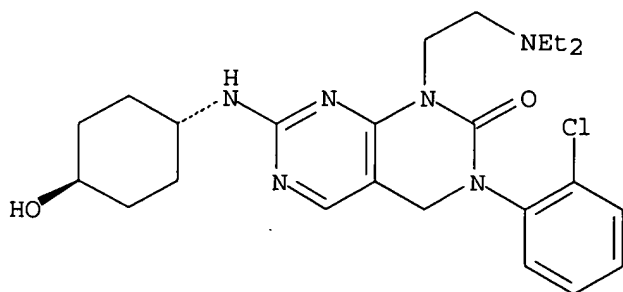


● HCl

RN 335653-01-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-1-[2-(diethylamino)ethyl]-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-, monohydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

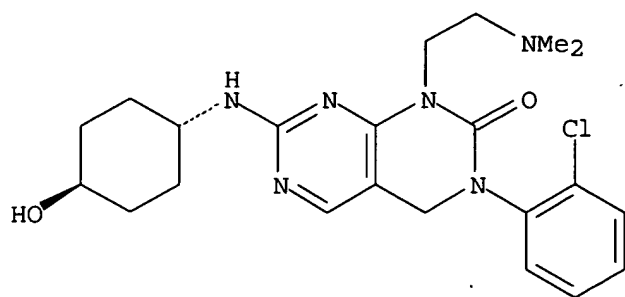


● HCl

RN 335653-02-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-1-[2-(dimethylamino)ethyl]-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-, monohydrochloride (9CI) (CA INDEX NAME)

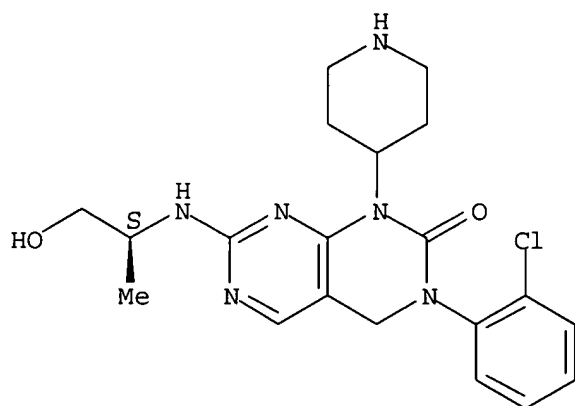
Relative stereochemistry.



● HCl

RN 335653-03-7 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-
 [[(1S)-2-hydroxy-1-methylethyl]amino]-1-(4-piperidinyl)-,
 monohydrochloride (9CI) (CA INDEX NAME)

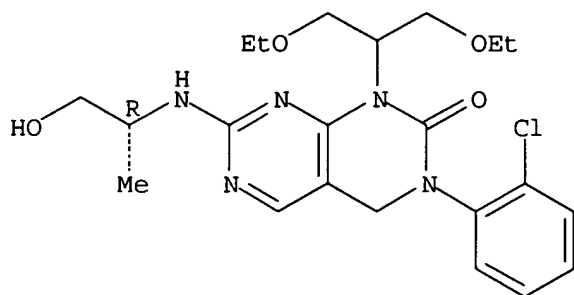
Absolute stereochemistry.



● HCl

RN 335653-04-8 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-1-[2-ethoxy-1-
 (ethoxymethyl)ethyl]-3,4-dihydro-7-[[(1R)-2-hydroxy-1-methylethyl]amino]-,
 monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

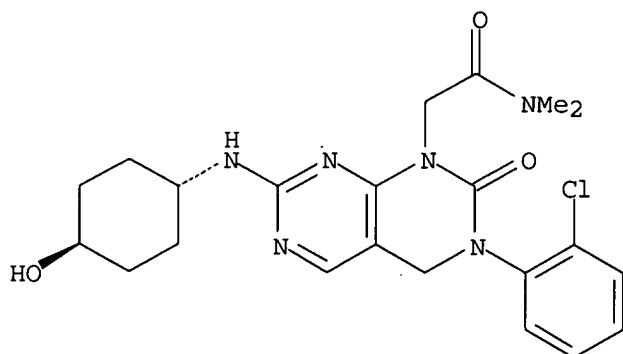


● HCl

RN 335653-05-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetamide, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-N,N-dimethyl-2-oxo-, monohydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

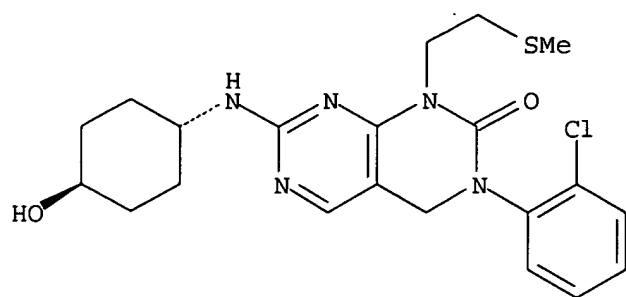


● HCl

RN 335653-22-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-1-[2-(methylthio)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

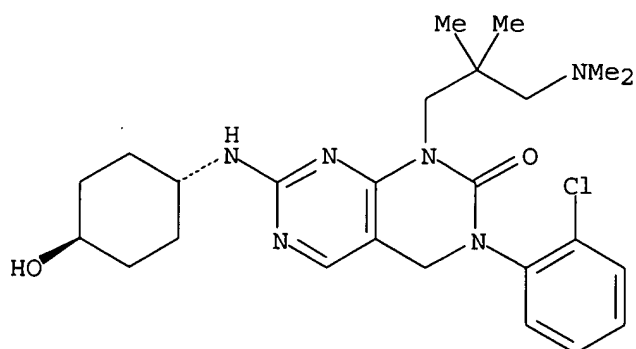


● HCl

RN 335653-23-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-1-[3-(dimethylamino)-2,2-dimethylpropyl]-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-, monohydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

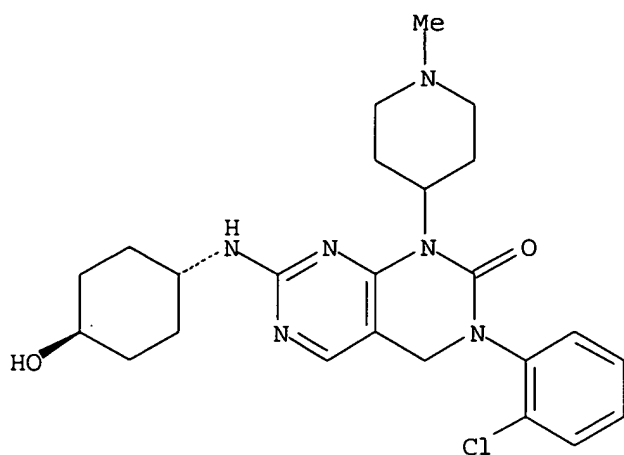


● HCl

RN 335653-24-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(trans-4-hydroxycyclohexyl)amino]-1-(1-methyl-4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

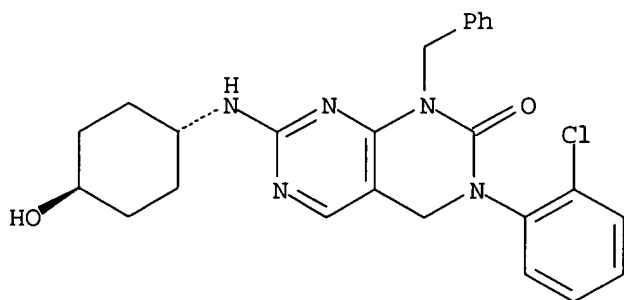
Relative stereochemistry.



● HCl

RN 335653-37-7 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-
 [(trans-4-hydroxycyclohexyl)amino]-1-(phenylmethyl)-, monohydrochloride
 (9CI) (CA INDEX NAME)

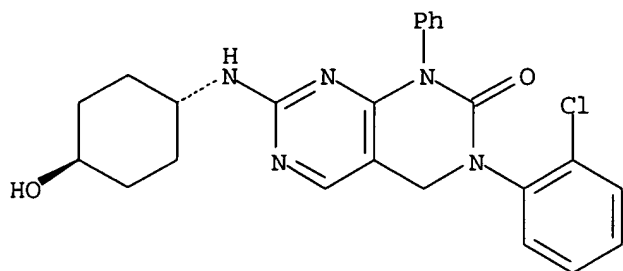
Relative stereochemistry.



● HCl

RN 335653-38-8 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-
 [(trans-4-hydroxycyclohexyl)amino]-1-phenyl-, monohydrochloride (9CI) (CA
 INDEX NAME)

Relative stereochemistry.



● HCl

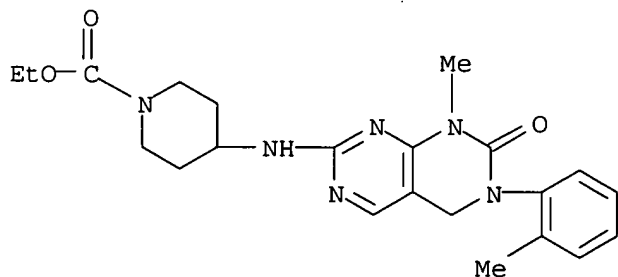
IT 335653-41-3P 335653-74-2P 335653-77-5P
335653-78-6P 335653-79-7P 335653-80-0P
335653-84-4P 335653-85-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of alkylamino substituted pyrimidino[4,5-d]pyrimidines for pharmaceutical use as inhibitors of p38 protein kinase)

RN 335653-41-3 HCAPLUS

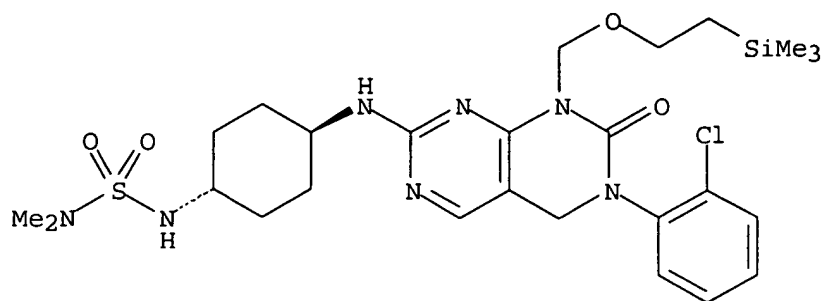
CN 1-Piperidinecarboxylic acid, 4-[[1,5,6,7-tetrahydro-8-methyl-6-(2-methylphenyl)-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



RN 335653-74-2 HCAPLUS

CN Sulfamide, N'-[trans-4-[[6-(2-chlorophenyl)-5,6,7,8-tetrahydro-7-oxo-8-[[2-(trimethylsilyl)ethoxy]methyl]pyrimido[4,5-d]pyrimidin-2-yl]amino]cyclohexyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

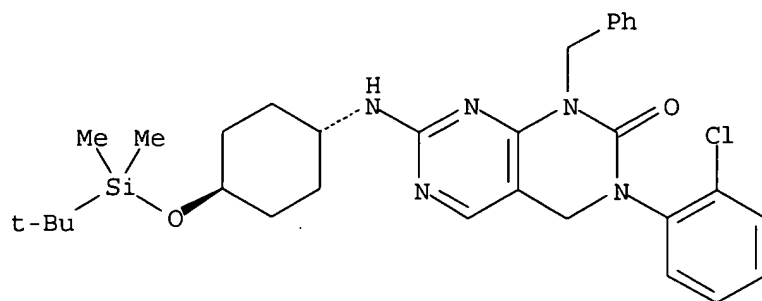
Relative stereochemistry.



RN 335653-77-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-7-[[trans-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]cyclohexyl]amino]-3,4-dihydro-1-(phenylmethyl)- (9CI) (CA INDEX NAME)

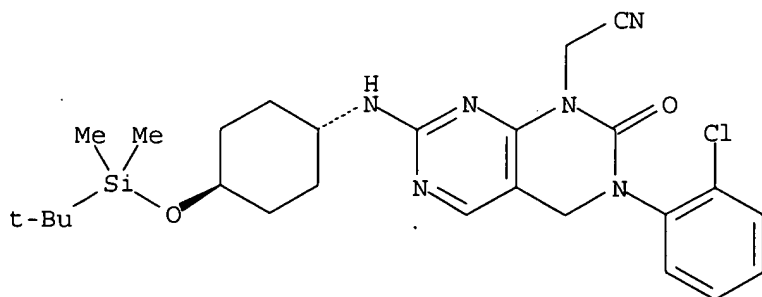
Relative stereochemistry.



RN 335653-78-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetonitrile, 3-(2-chlorophenyl)-7-[[trans-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]cyclohexyl]amino]-3,4-dihydro-2-oxo- (9CI) (CA INDEX NAME)

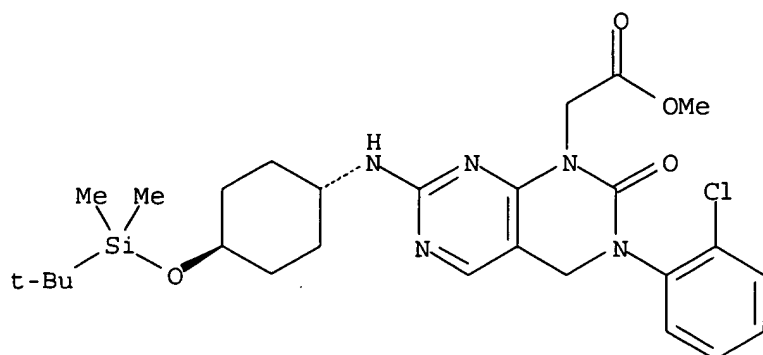
Relative stereochemistry.



RN 335653-79-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetic acid, 3-(2-chlorophenyl)-7-[[trans-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]cyclohexyl]amino]-3,4-dihydro-2-oxo-, methyl ester (9CI) (CA INDEX NAME)

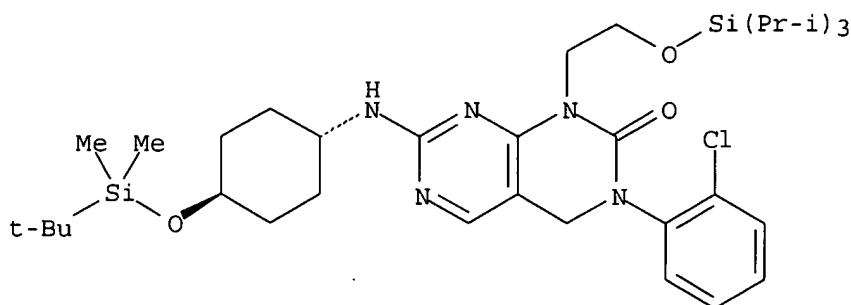
Relative stereochemistry.



RN 335653-80-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-7-[[trans-4-[[1,1-dimethylethyl]dimethylsilyl]oxy]cyclohexyl]amino]-3,4-dihydro-1-[2-[[tris(1-methylethyl)silyl]oxy]ethyl]- (9CI) (CA INDEX NAME)

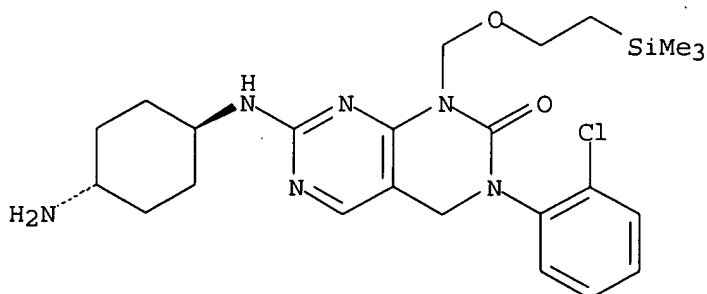
Relative stereochemistry.



RN 335653-84-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[(trans-4-aminocyclohexyl)amino]-3-(2-chlorophenyl)-3,4-dihydro-1-[[2-(trimethylsilyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)

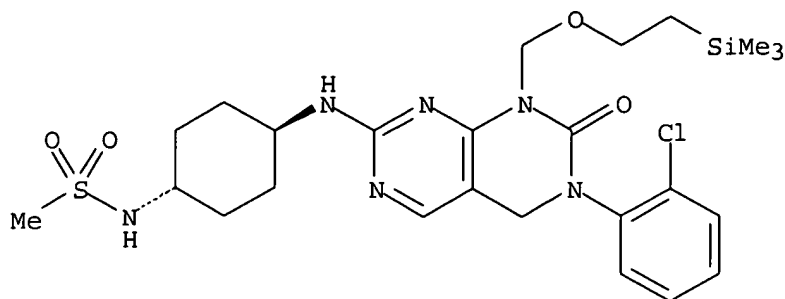
Relative stereochemistry.



RN 335653-85-5 HCAPLUS

CN Methanesulfonamide, N-[trans-4-[[6-(2-chlorophenyl)-5,6,7,8-tetrahydro-7-oxo-8-[[2-(trimethylsilyl)ethoxy]methyl]pyrimido[4,5-d]pyrimidin-2-yl]amino]cyclohexyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:300720 HCAPLUS

DOCUMENT NUMBER: 134:311223

TITLE: Preparation of alkylamino substituted bicyclic nitrogen heterocycles for pharmaceutical use as inhibitors of p38 protein kinase

INVENTOR(S): Dunn, James Patrick; Goldstein, David Michael; Harris, William; Smith, Ian Edward David; Welch, Teresa Rosanne

PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.

SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

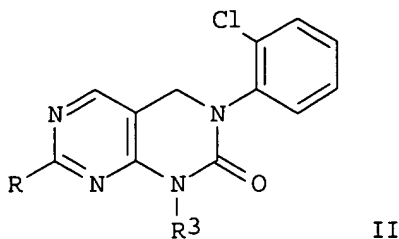
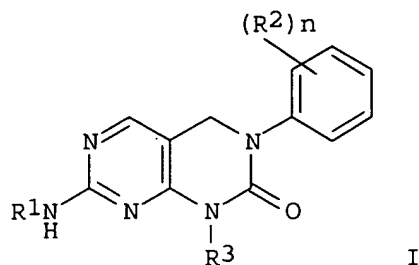
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|------------|
| WO 2001029041 | A1 | 20010426 | WO 2000-EP10077 | 20001013 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2388140 | AA | 20010426 | CA 2000-2388140 | 20001013 |
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| TR 200201058 | T2 | 20020722 | TR 2002-200201058 | 20001013 |
| EP 1226144 | A1 | 20020731 | EP 2000-972755 | 20001013 |
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| JP 2003512377 | T2 | 20030402 | JP 2001-531839 | 20001013 |
| AU 776695 | B2 | 20040916 | AU 2001-11375 | 20001013 |
| US 6642241 | B1 | 20031104 | US 2000-693364 | 20001020 |
| ZA 2002002603 | A | 20030703 | ZA 2002-2603 | 20020403 |
| NO 2002001783 | A | 20020416 | NO 2002-1783 | 20020416 |
| PRIORITY APPLN. INFO.: | | | US 1999-160804P | P 19991021 |
| | | | US 2000-213718P | P 20000622 |

WO 2000-EP10077

W 20001013

OTHER SOURCE(S):
GI

MARPAT 134:311223



AB Alkylamino-substituted dihydropyrimido[4,5-d]pyrimidinone derivs., such as I [R1 = H, alkyl, alkenyl, alkynyl, acyl, cycloalkyl, etc.; R2 = vinyl, alkyl, halogen, heteroalkyl; R3 = alkyl, heteroalkyl, cycloalkyl, heterocyclyl, etc.; n = 0-3], were prepared for pharmaceutical use as inhibitors of p38 protein kinase for the treatment of conditions such as arthritis, Crohn's disease, obstructive pulmonary disease, or irritable bowel syndrome.. Thus, dihydropyrimido[4,5-d]pyrimidinone II (R = NHCHMe2, R3 = CH2CO2H) was prepared via a substitution reaction of H2NCHMe2 with sulfone II (R = SO2CH2Ph, R3 = CH2CO2Et) when combined and heated to 90-100° for 1 h. The prepared dihydropyrimido[4,5-d]pyrimidinone derivs. showed p38 50% inhibitory activity at concns. < 10 µM.

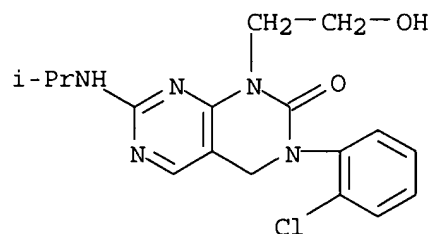
IT 335318-15-5P 335318-19-9P 335318-22-4P
335318-39-3P 335318-40-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of alkylamino substituted pyrimidino[4,5-d]pyrimidines for pharmaceutical use as inhibitors of p38 protein kinase)

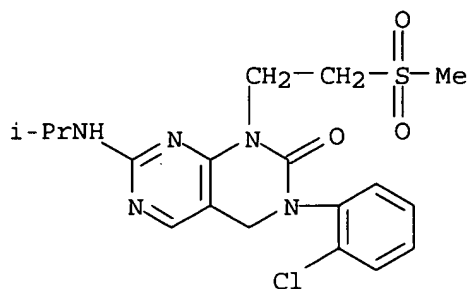
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CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-1-(2-hydroxyethyl)-7-[(1-methylethyl)amino]- (9CI) (CA INDEX NAME)



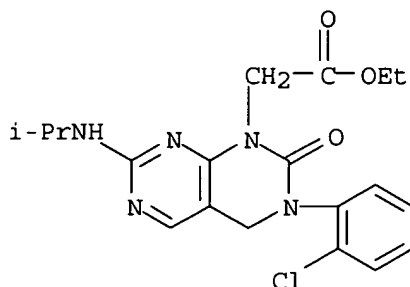
RN 335318-19-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(1-methylethyl)amino]-1-[2-(methylsulfonyl)ethyl]- (9CI) (CA INDEX NAME)



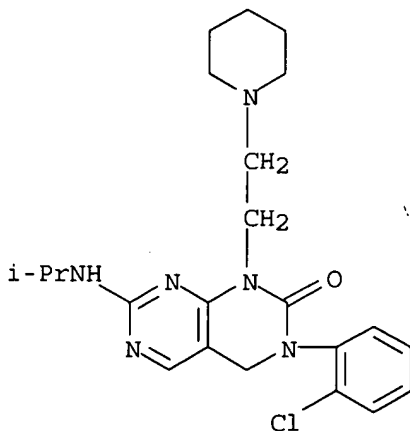
RN 335318-22-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetic acid, 3-(2-chlorophenyl)-3,4-dihydro-7-[(1-methylethyl)amino]-2-oxo-, ethyl ester (9CI) (CA INDEX NAME)



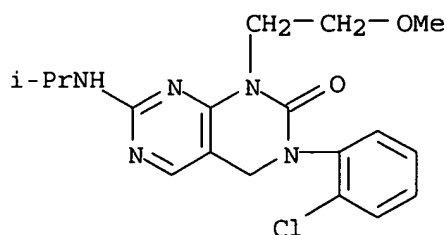
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CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(1-methylethyl)amino]-1-[2-(1-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 335318-40-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-1-(2-methoxyethyl)-7-[(1-methylethyl)amino]- (9CI) (CA INDEX NAME)

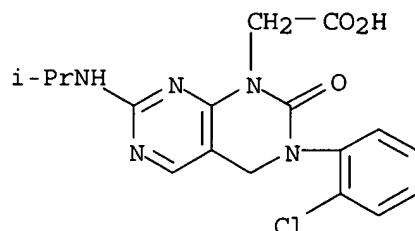


IT 335318-09-7P 335318-10-0P 335318-11-1P
335318-12-2P 335318-16-6P 335318-17-7P
335318-18-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of alkylamino substituted pyrimidino[4,5-d]pyrimidines for pharmaceutical use as inhibitors of p38 protein kinase)

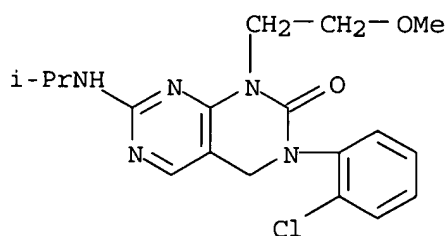
RN 335318-09-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-1(2H)-acetic acid, 3-(2-chlorophenyl)-3,4-dihydro-7-[(1-methylethyl)amino]-2-oxo- (9CI) (CA INDEX NAME)



RN 335318-10-0 HCAPLUS

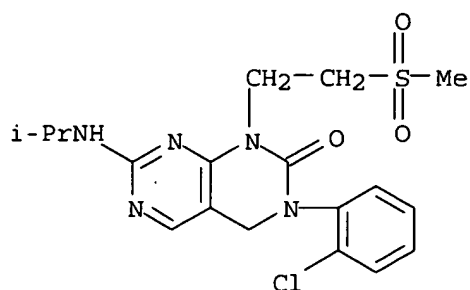
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-1-(2-methoxyethyl)-7-[(1-methylethyl)amino]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

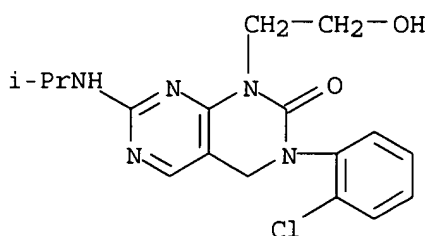
RN 335318-11-1 HCAPLUS

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● HCl

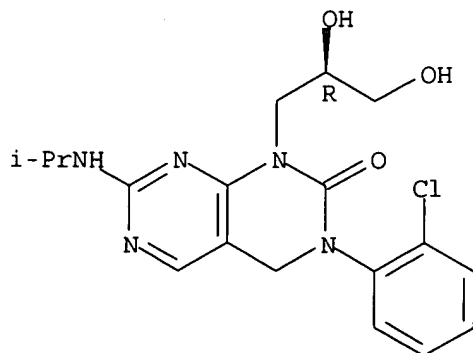
RN 335318-12-2 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-1-[(1-methylethyl)amino]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 335318-16-6 HCAPLUS
 CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-1-[(2R)-2,3-dihydroxypropyl]-3,4-dihydro-7-[(1-methylethyl)amino]- (9CI) (CA INDEX NAME)

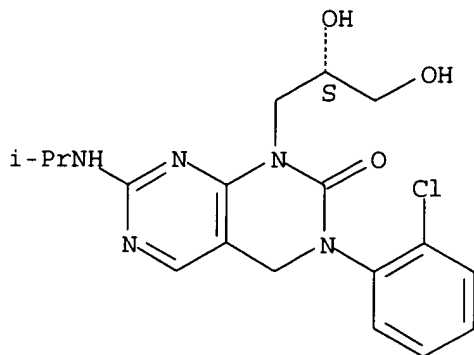
Absolute stereochemistry.



RN 335318-17-7 HCAPLUS

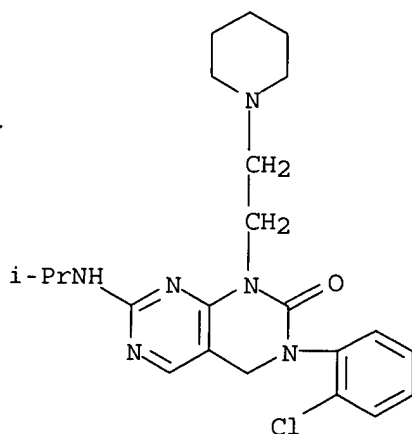
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-1-[(2S)-2,3-dihydroxypropyl]-3,4-dihydro-7-[(1-methylethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 335318-18-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(1-methylethyl)amino]-1-[2-(1-piperidinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

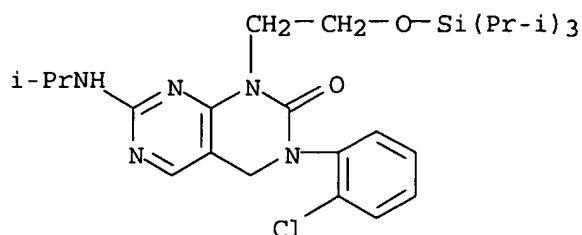
IT 335318-27-9P 335318-33-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of alkylamino substituted pyrimidino[4,5-d]pyrimidines for pharmaceutical use as inhibitors of p38 protein kinase)

RN 335318-27-9 HCAPLUS

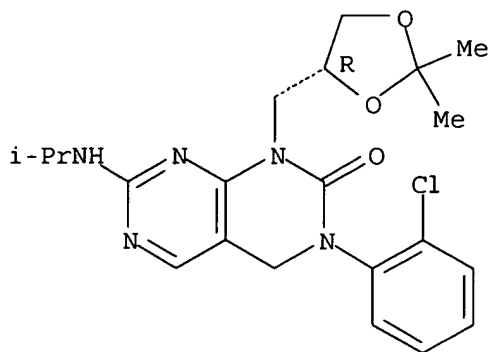
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-3,4-dihydro-7-[(1-methylethyl)amino]-1-[2-[[tris(1-methylethyl)silyl]oxy]ethyl]- (9CI) (CA INDEX NAME)



RN 335318-33-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-1-[[[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]methyl]-3,4-dihydro-7-[(1-methylethyl)amino]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:291041 HCAPLUS

DOCUMENT NUMBER: 132:308352

TITLE: Preparation of pyrimidopyrimidinones as T-cell tyrosine kinase inhibitors

INVENTOR(S): Harris, William; Hill, Christopher Huw; Smith, Ian Edward David

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 109 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2000024744 | A1 | 20000504 | WO 1999-EP7675 | 19991013 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|------------|----|----------|-----------------|----------|
| CA 2347474 | AA | 20000504 | CA 1999-2347474 | 19991013 |
| BR 9914677 | A | 20010717 | BR 1999-14677 | 19991013 |
| EP 1123295 | A1 | 20010816 | EP 1999-953796 | 19991013 |
| EP 1123295 | B1 | 20040929 | | |

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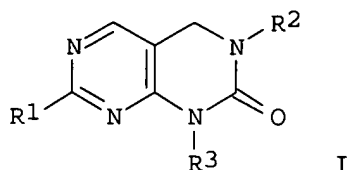
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| TR 200101102 | T2 | 20020121 | TR 2001-200101102 | 19991013 |
| JP 2002528455 | T2 | 20020903 | JP 2000-578314 | 19991013 |
| JP 3593035 | B2 | 20041124 | | |
| NZ 510760 | A | 20030829 | NZ 1999-510760 | 19991013 |
| AU 769989 | B2 | 20040212 | AU 2000-10363 | 19991013 |
| AT 277931 | E | 20041015 | AT 1999-953796 | 19991013 |
| US 6150373 | A | 20001121 | US 1999-422451 | 19991021 |
| ZA 2001002652 | A | 20020930 | ZA 2001-2652 | 20010330 |
| HR 2001000274 | A1 | 20020630 | HR 2001-274 | 20010412 |
| NO 2001001929 | A | 20010419 | NO 2001-1929 | 20010419 |
| HK 1041483 | A1 | 20041224 | HK 2002-103084 | 20020424 |

PRIORITY APPLN. INFO.:

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|----------------|---|----------|
| GB 1998-23277 | A | 19981023 |
| GB 1999-20044 | A | 19990824 |
| WO 1999-EP7675 | W | 19991013 |

OTHER SOURCE(S): MARPAT 132:308352

GI



AB Title compds. [I; R1 = NH₂, alkylamino, (hetero)aryl(alkyl)amino; R2 = alkyl (hetero)aryl(alkyl); R3 = H, alkyl, (hetero)aryl(alkyl), cycloalkenyl] were prepared. Thus, Et 4-chloro-2-methylthiopyrimidine-5-carboxylate was aminated by MeNH₂ and the product converted to the aldehyde which was condensed with 2,6-Cl₂C₆H₃NH₂ to give 2,6-Cl₂C₆H₃NHCH₂ZNHMe (Z = 2-methylthiopyrimidine-5,4-diyl). The latter was cyclocondensed with COCl₂ and the product oxidized to give I (R2 = 2,6-Cl₂C₆H₃NHCH₂, R3 = Me) (II; R1 = SO₂Me) which was aminated by 4-(H₂N)C₆H₄OCH₂CH₂NEt₂ (preparation given) to give II [R1 = 4-(Et₂NCH₂CH₂O)C₆H₄NH]. Data for biol. activity of I were given.

IT 266312-86-1P 266312-87-2P 266312-88-3P
 266312-93-0P 266312-94-1P 266312-95-2P
 266312-97-4P 266312-98-5P 266312-99-6P
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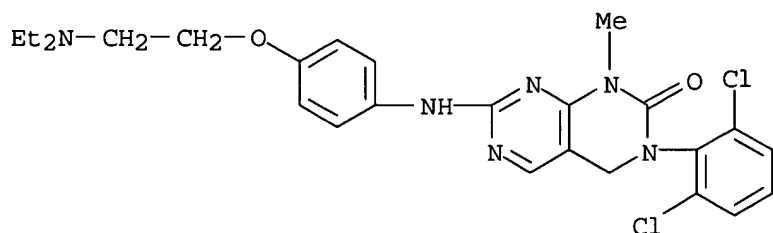
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 266313-77-3P 266313-78-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrimidopyrimidinones as T-cell tyrosine kinase inhibitors)

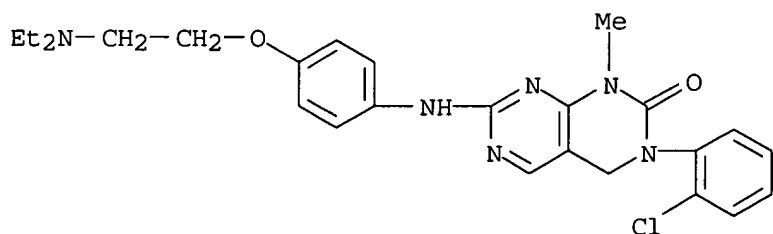
RN 266312-86-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



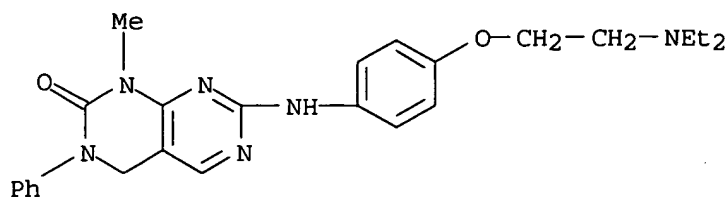
RN 266312-87-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chlorophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



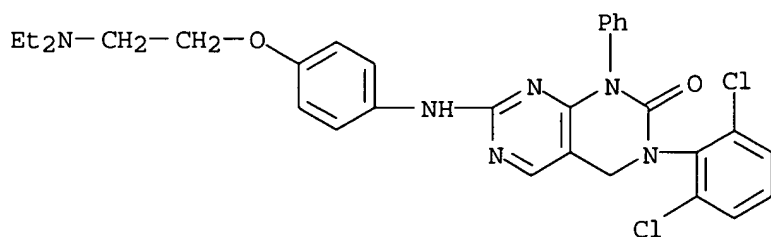
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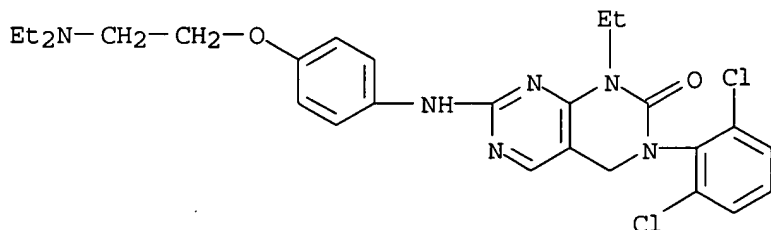
RN 266312-93-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-phenyl- (9CI) (CA INDEX NAME)



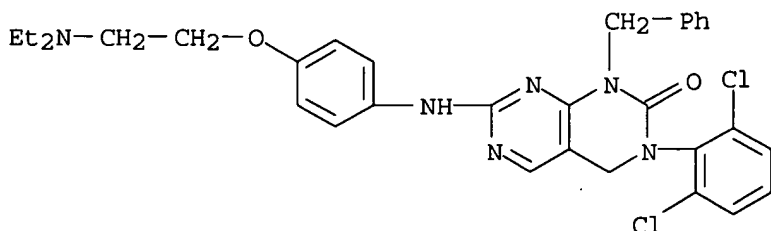
RN 266312-94-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 266312-95-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



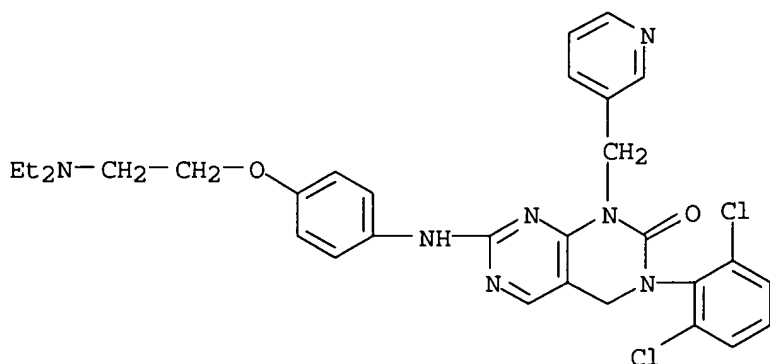
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CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-(3-pyridinylmethyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

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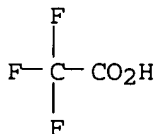
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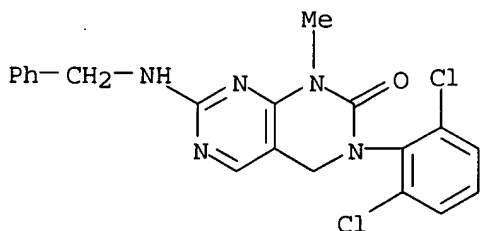
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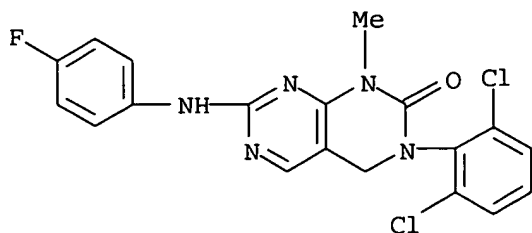
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CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-3,4-dihydro-1-methyl-7-[(phenylmethyl)amino] - (9CI) (CA INDEX NAME)



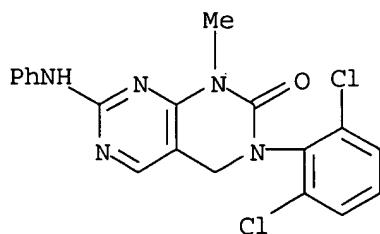
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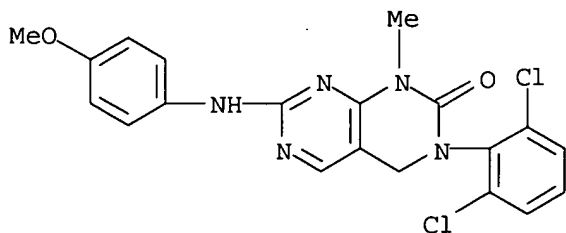
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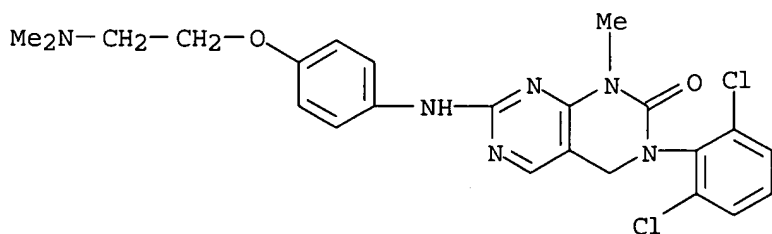
RN 266313-01-3 HCAPLUS

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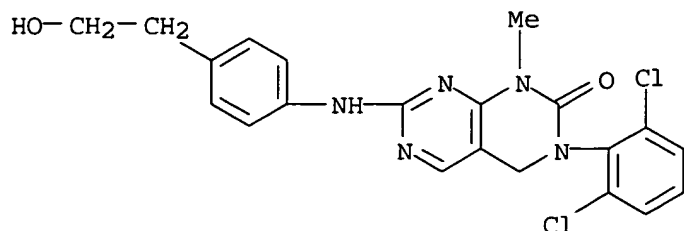
RN 266313-02-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-7-[[4-[2-(dimethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



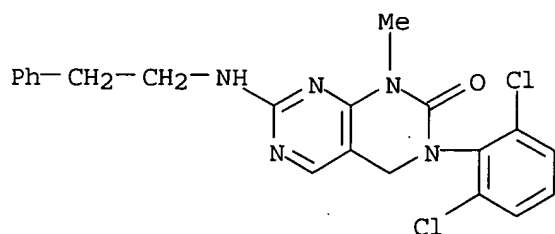
RN 266313-03-5 HCAPLUS

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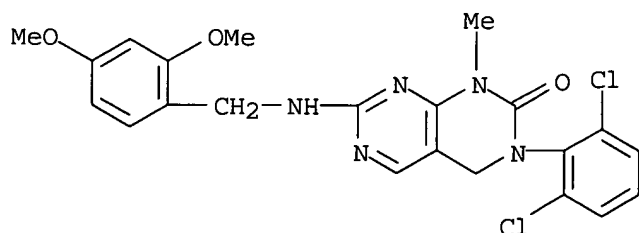
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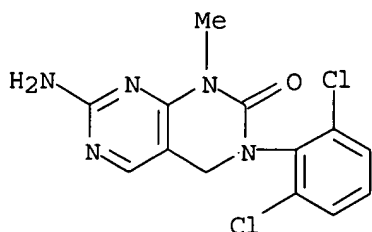
RN 266313-05-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-7-[[(2,4-dimethoxyphenyl)methyl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 266313-06-8 HCAPLUS

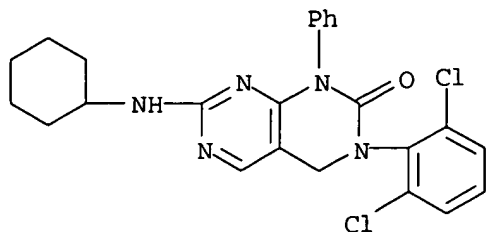
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-amino-3-(2,6-dichlorophenyl)-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 266313-07-9 HCAPLUS

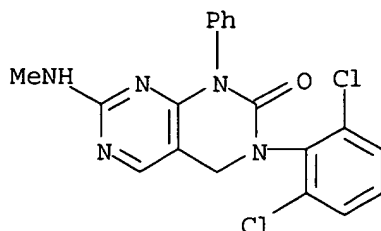
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-(cyclohexylamino)-3-(2,6-

dichlorophenyl)-3,4-dihydro-1-phenyl- (9CI) (CA INDEX NAME)



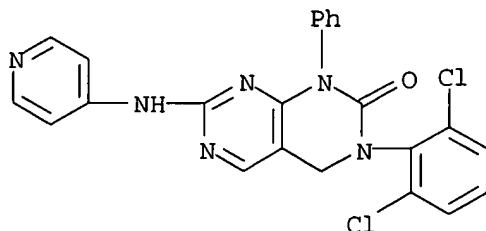
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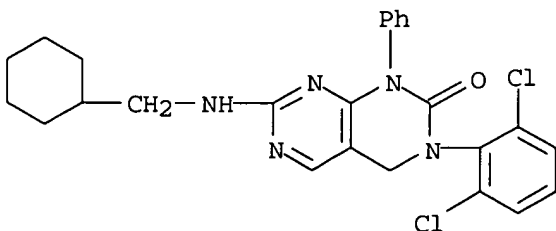
RN 266313-09-1 HCAPLUS

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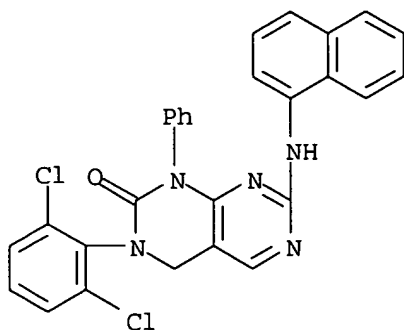
RN 266313-10-4 HCAPLUS

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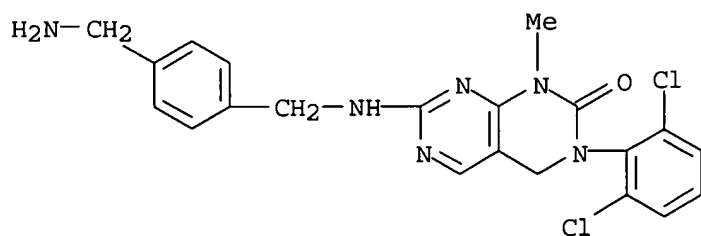
RN 266313-11-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-3,4-dihydro-7-(1-naphthalenylamino)-1-phenyl- (9CI) (CA INDEX NAME)



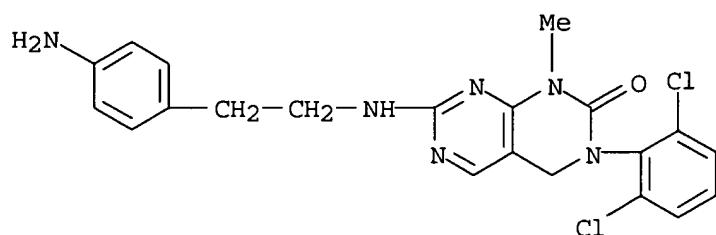
RN 266313-12-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[[4-(aminomethyl)phenyl]methyl]amino]-3-(2,6-dichlorophenyl)-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



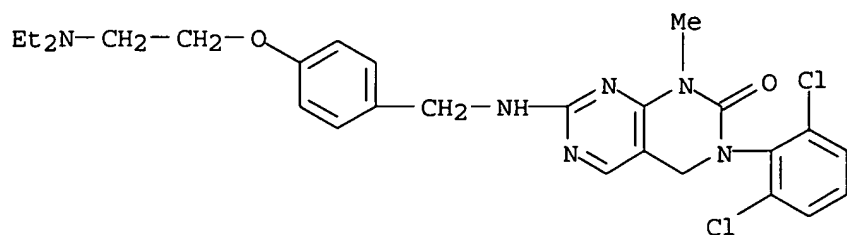
RN 266313-13-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[2-(4-aminophenyl)ethyl]amino]-3-(2,6-dichlorophenyl)-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



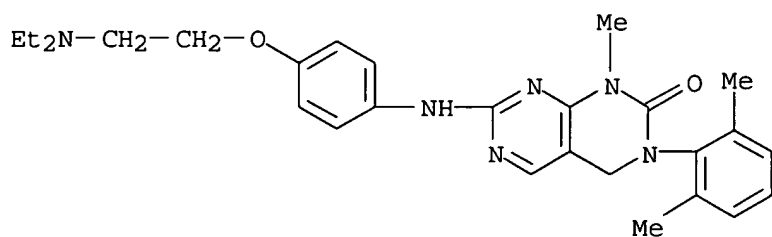
RN 266313-14-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-7-[[[4-[2-(diethylamino)ethoxy]phenyl]methyl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



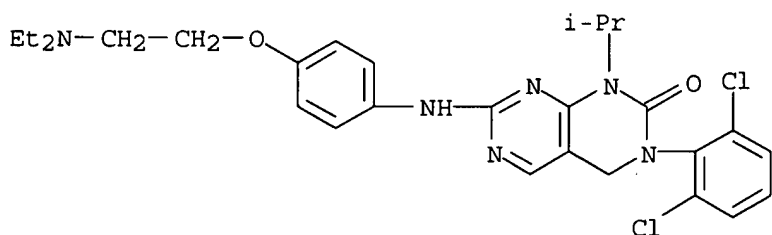
RN 266313-15-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3-(2,6-dimethylphenyl)-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



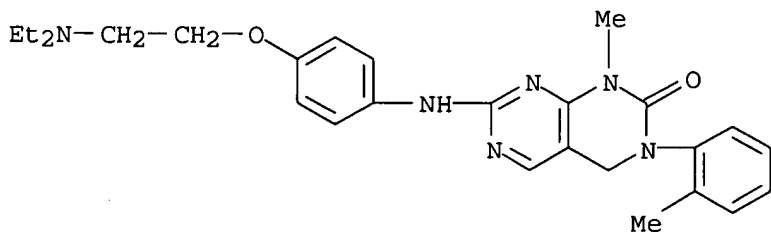
RN 266313-17-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 266313-18-2 HCAPLUS

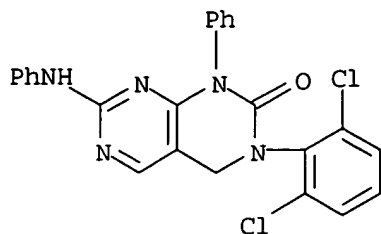
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-methyl-3-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 266313-19-3 HCAPLUS

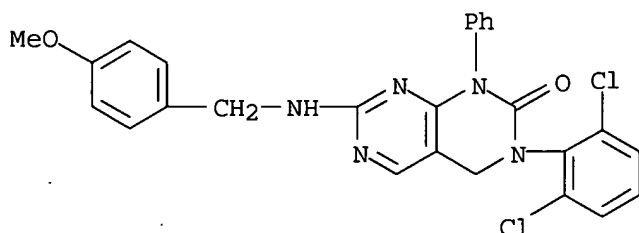
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-3,4-dihydro-1-

phenyl-7-(phenylamino)- (9CI) (CA INDEX NAME)



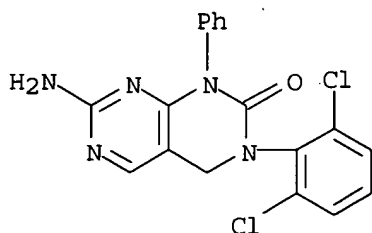
RN 266313-20-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-3,4-dihydro-7-[[4-methoxyphenyl)methyl]amino]-1-phenyl- (9CI) (CA INDEX NAME)



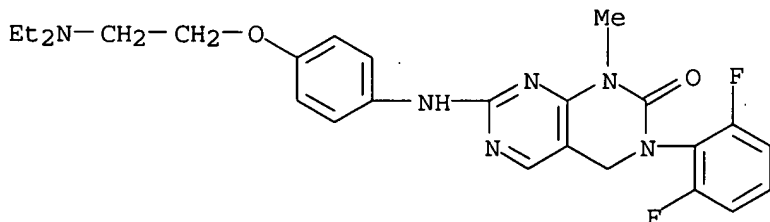
RN 266313-21-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-amino-3-(2,6-dichlorophenyl)-3,4-dihydro-1-phenyl- (9CI) (CA INDEX NAME)



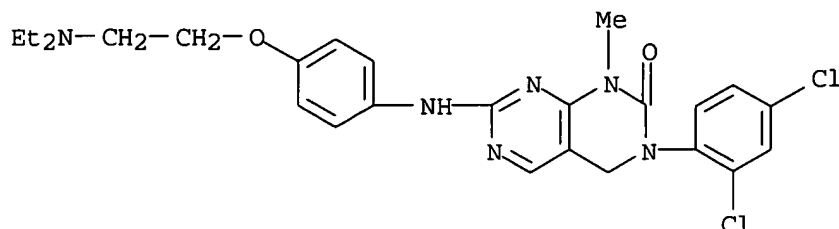
RN 266313-22-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3-(2,6-difluorophenyl)-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



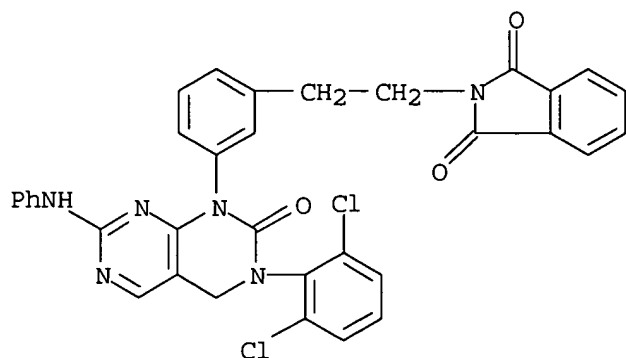
RN 266313-23-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,4-dichlorophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



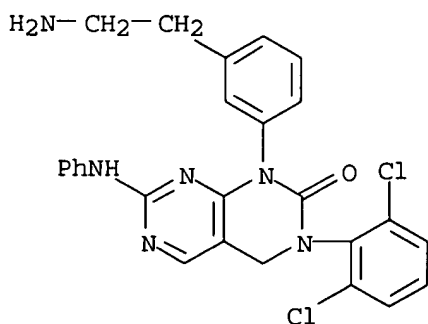
RN 266313-24-0 HCAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[3-[3-(2,6-dichlorophenyl)-3,4-dihydro-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]phenyl]ethyl]- (9CI) (CA INDEX NAME)



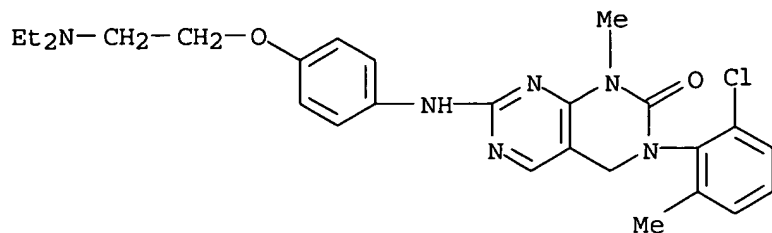
RN 266313-25-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[3-(2-aminoethyl)phenyl]-3-(2,6-dichlorophenyl)-3,4-dihydro-7-(phenylamino)- (9CI) (CA INDEX NAME)



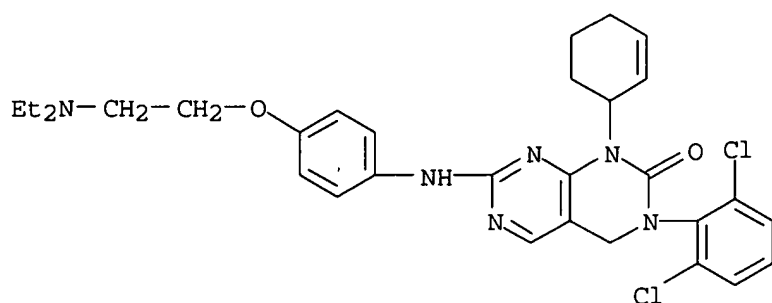
RN 266313-27-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chloro-6-methylphenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



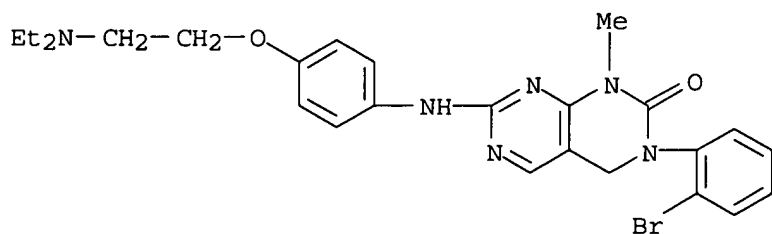
RN 266313-29-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-(2-cyclohexen-1-yl)-3-(2,6-dichlorophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-(9CI) (CA INDEX NAME)



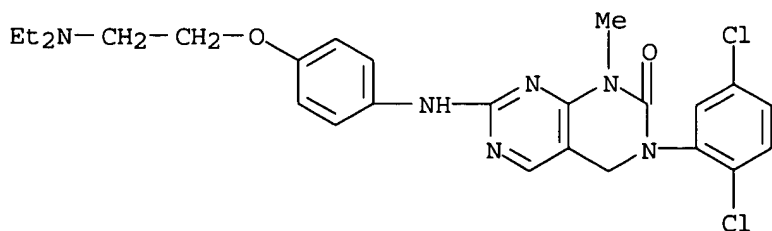
RN 266313-30-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



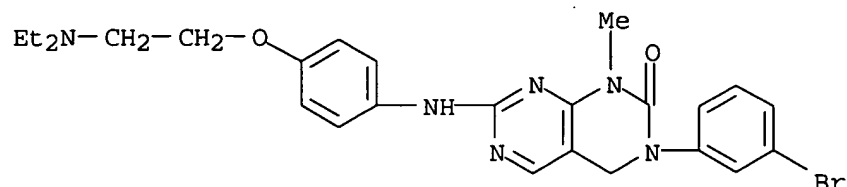
RN 266313-31-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,5-dichlorophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



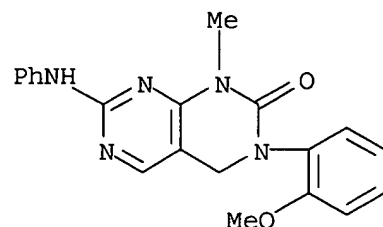
RN 266313-32-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(3-bromophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



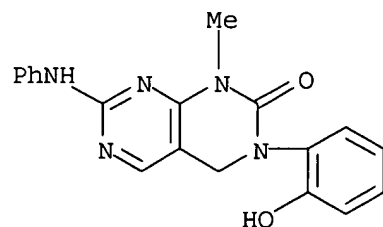
RN 266313-33-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-3-(2-methoxyphenyl)-1-methyl-7-(phenylamino)- (9CI) (CA INDEX NAME)



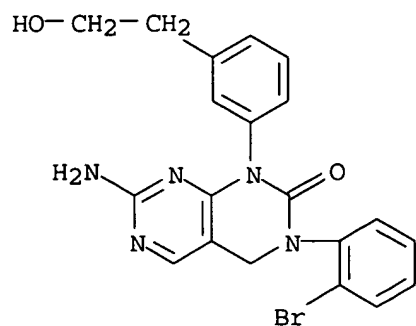
RN 266313-34-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3,4-dihydro-3-(2-hydroxyphenyl)-1-methyl-7-(phenylamino)- (9CI) (CA INDEX NAME)



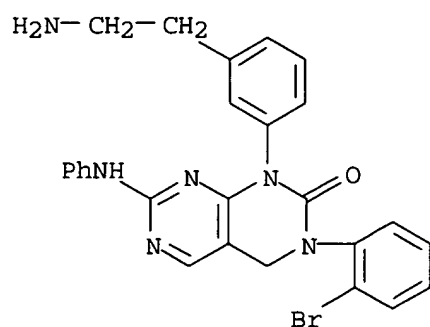
RN 266313-36-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-amino-3-(2-bromophenyl)-3,4-dihydro-1-[3-(2-hydroxyethyl)phenyl]- (9CI) (CA INDEX NAME)



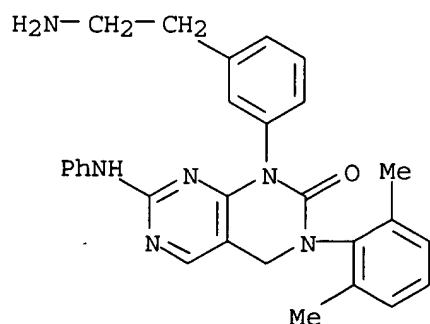
RN 266313-37-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[3-(2-aminoethyl)phenyl]-3-(2-bromophenyl)-3,4-dihydro-7-(phenylamino)- (9CI) (CA INDEX NAME)



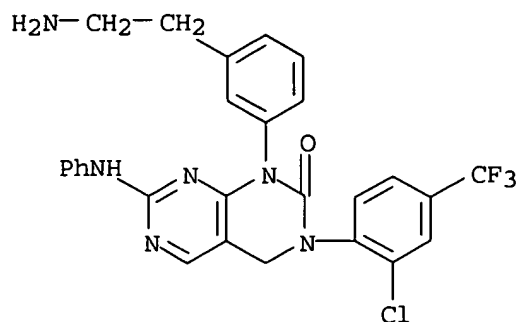
RN 266313-38-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[3-(2-aminoethyl)phenyl]-3-(2,6-dimethylphenyl)-3,4-dihydro-7-(phenylamino)- (9CI) (CA INDEX NAME)



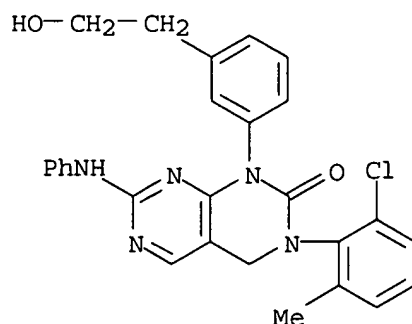
RN 266313-39-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[3-(2-aminoethyl)phenyl]-3-[2-chloro-4-(trifluoromethyl)phenyl]-3,4-dihydro-7-(phenylamino)- (9CI) (CA INDEX NAME)



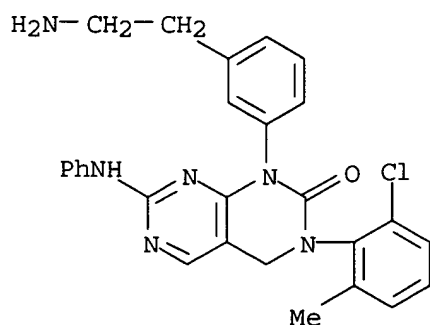
RN 266313-40-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chloro-6-methylphenyl)-3,4-dihydro-1-[3-(2-hydroxyethyl)phenyl]-7-(phenylamino)- (9CI) (CA INDEX NAME)



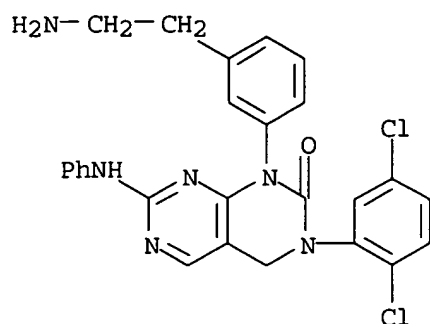
RN 266313-41-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[3-(2-aminoethyl)phenyl]-3-(2-chloro-6-methylphenyl)-3,4-dihydro-7-(phenylamino)- (9CI) (CA INDEX NAME)



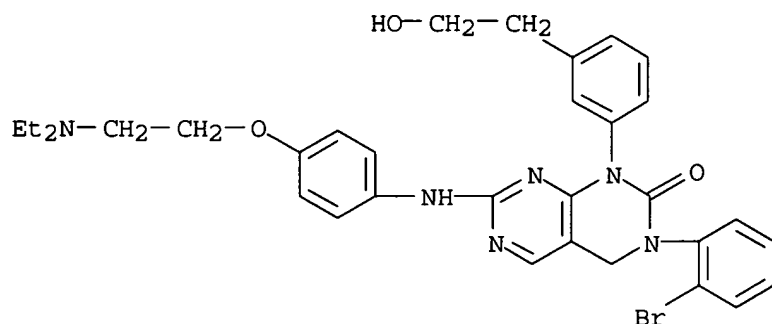
RN 266313-42-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[3-(2-aminoethyl)phenyl]-3-(2,5-dichlorophenyl)-3,4-dihydro-7-(phenylamino)- (9CI) (CA INDEX NAME)



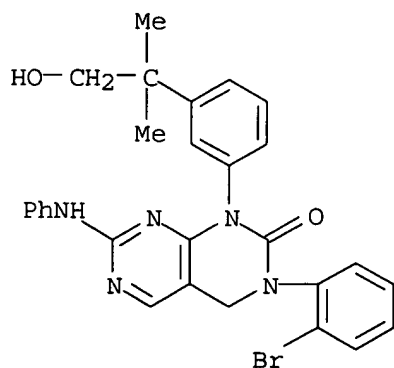
RN 266313-43-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-[3-(2-hydroxyethyl)phenyl]- (9CI) (CA INDEX NAME)



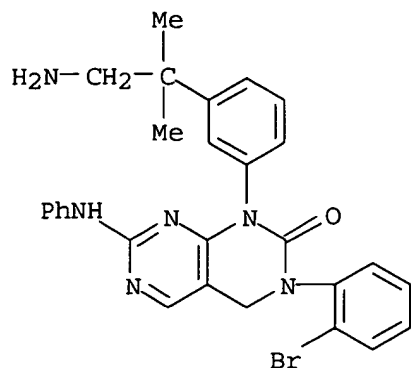
RN 266313-44-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-3,4-dihydro-1-[3-(2-hydroxy-1,1-dimethylethyl)phenyl]-7-(phenylamino)- (9CI) (CA INDEX NAME)



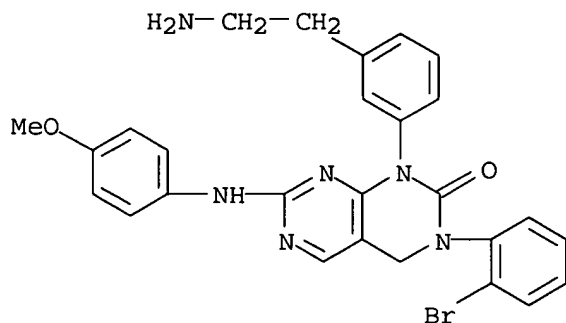
RN 266313-45-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[3-(2-amino-1,1-dimethylethyl)phenyl]-3-(2-bromophenyl)-3,4-dihydro-7-(phenylamino)- (9CI) (CA INDEX NAME)



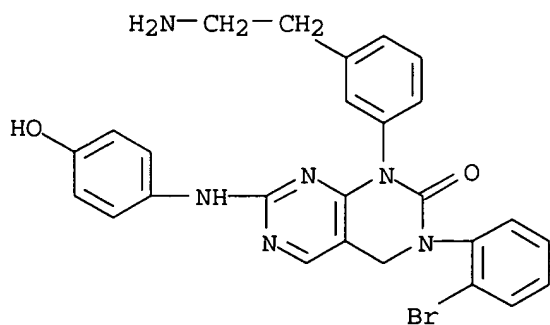
RN 266313-46-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[3-(2-aminoethyl)phenyl]-3-(2-bromophenyl)-3,4-dihydro-7-[(4-methoxyphenyl)amino]- (9CI) (CA INDEX NAME)



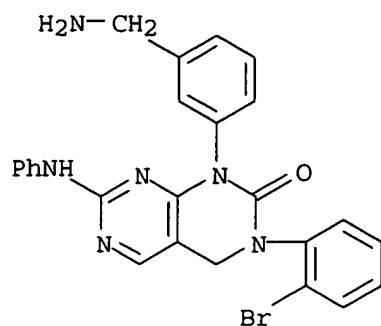
RN 266313-47-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[3-(2-aminoethyl)phenyl]-3-(2-bromophenyl)-3,4-dihydro-7-[(4-hydroxyphenyl)amino]- (9CI) (CA INDEX NAME)



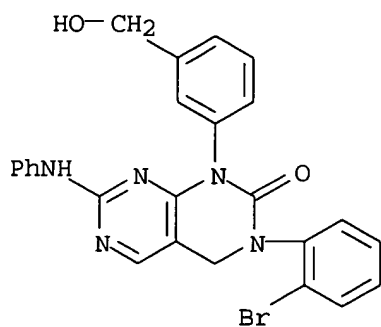
RN 266313-48-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[3-(aminomethyl)phenyl]-3-(2-bromophenyl)-3,4-dihydro-7-(phenylamino)- (9CI) (CA INDEX NAME)



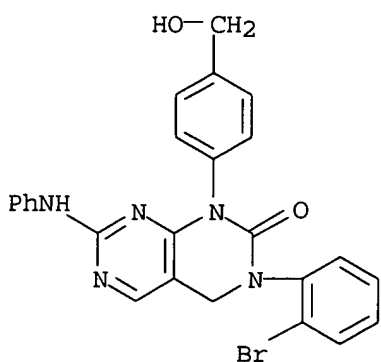
RN 266313-49-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-3,4-dihydro-1-[3-(hydroxymethyl)phenyl]-7-(phenylamino)- (9CI) (CA INDEX NAME)



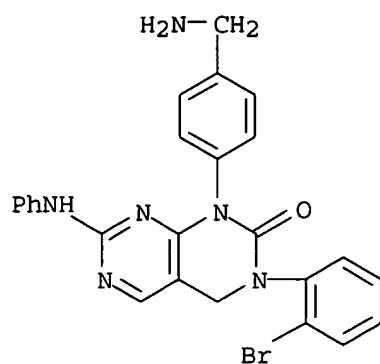
RN 266313-50-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-3,4-dihydro-1-[4-(hydroxymethyl)phenyl]-7-(phenylamino)- (9CI) (CA INDEX NAME)



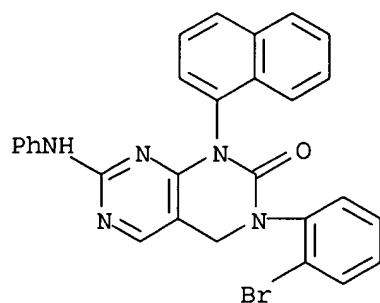
RN 266313-51-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[4-(aminomethyl)phenyl]-3-(2-bromophenyl)-3,4-dihydro-7-(phenylamino)- (9CI) (CA INDEX NAME)



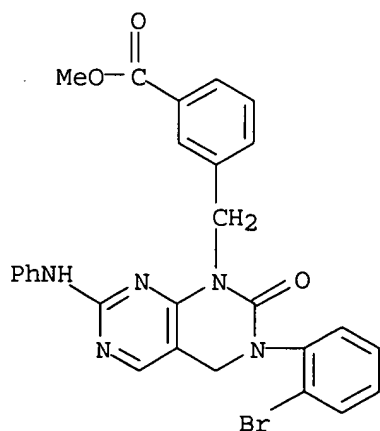
RN 266313-52-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-3,4-dihydro-1-(1-naphthalenyl)-7-(phenylamino)- (9CI) (CA INDEX NAME)



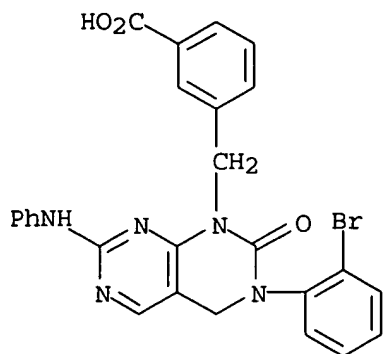
RN 266313-53-5 HCAPLUS

CN Benzoic acid, 3-[[3-(2-bromophenyl)-3,4-dihydro-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



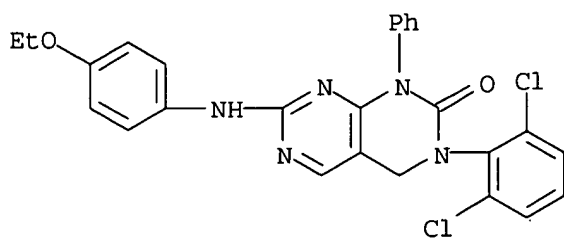
RN 266313-54-6 HCAPLUS

CN Benzoic acid, 3-[[3-(2-bromophenyl)-3,4-dihydro-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]methyl]- (9CI) (CA INDEX NAME)



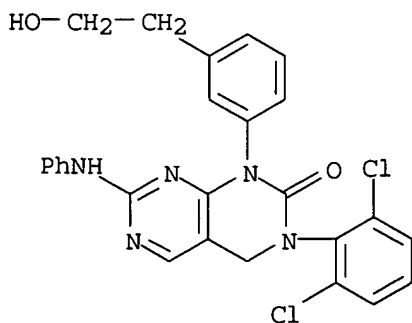
RN 266313-55-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-7-[(4-ethoxyphenyl)amino]-3,4-dihydro-1-phenyl- (9CI) (CA INDEX NAME)



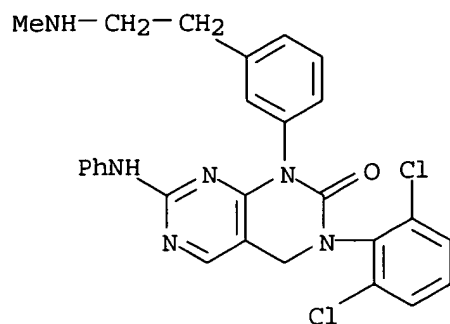
RN 266313-56-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-3,4-dihydro-1-[3-(2-hydroxyethyl)phenyl]-7-(phenylamino)- (9CI) (CA INDEX NAME)



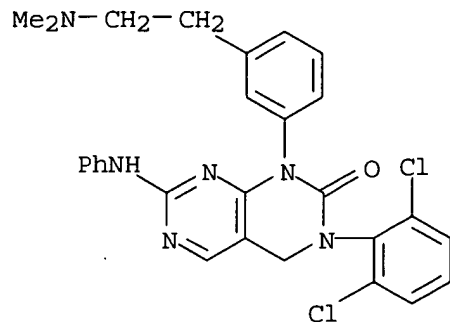
RN 266313-57-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-3,4-dihydro-1-[3-[2-(methylanino)ethyl]phenyl]-7-(phenylamino)- (9CI) (CA INDEX NAME)



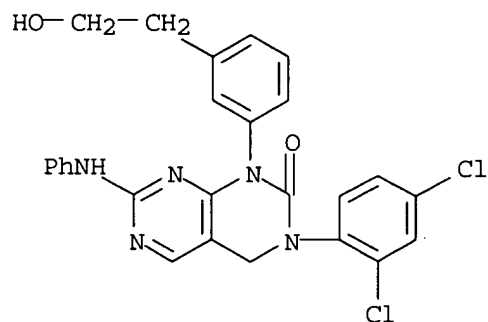
RN 266313-58-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-1-[3-[2-(dimethylamino)ethyl]phenyl]-3,4-dihydro-7-(phenylamino)- (9CI) (CA INDEX NAME)



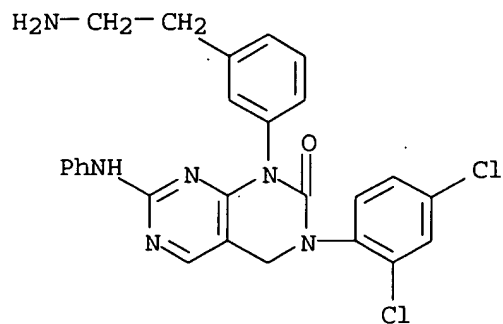
RN 266313-59-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,4-dichlorophenyl)-3,4-dihydro-1-[3-(2-hydroxyethyl)phenyl]-7-(phenylamino)- (9CI) (CA INDEX NAME)



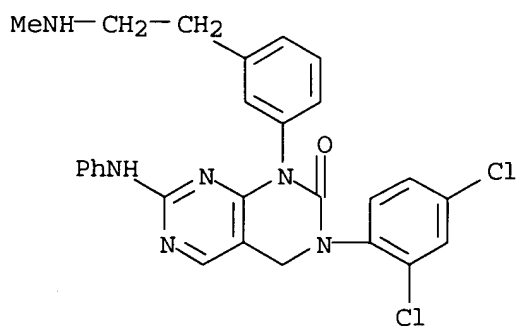
RN 266313-60-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[3-(2-aminoethyl)phenyl]-3-(2,4-dichlorophenyl)-3,4-dihydro-7-(phenylamino)- (9CI) (CA INDEX NAME)



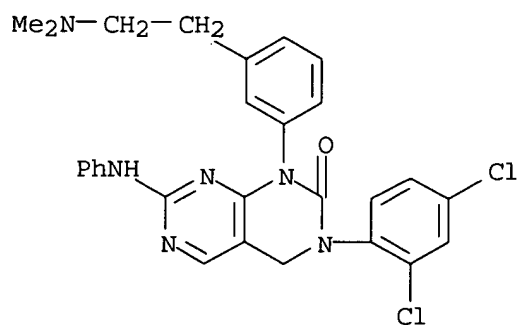
RN 266313-61-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,4-dichlorophenyl)-3,4-dihydro-1-[3-[2-(methylamino)ethyl]phenyl]-7-(phenylamino)- (9CI) (CA INDEX NAME)



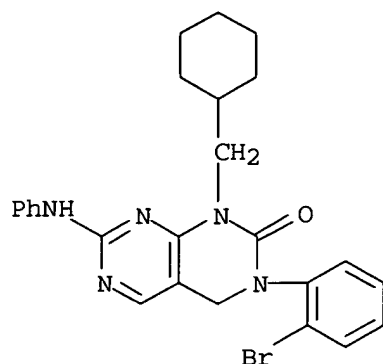
RN 266313-62-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,4-dichlorophenyl)-1-[3-[2-(dimethylamino)ethyl]phenyl]-3,4-dihydro-7-(phenylamino)- (9CI) (CA INDEX NAME)



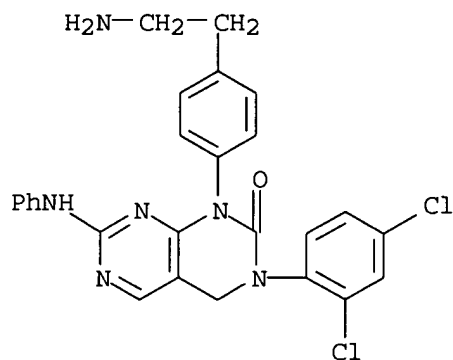
RN 266313-63-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-1-(cyclohexylmethyl)-3,4-dihydro-7-(phenylamino)- (9CI) (CA INDEX NAME)



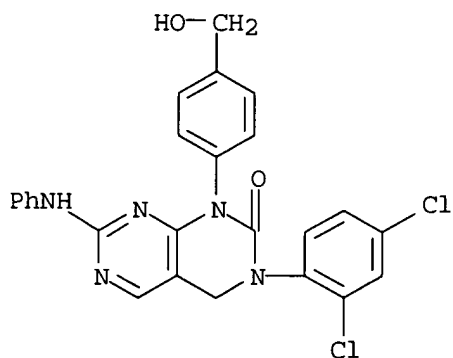
RN 266313-64-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[4-(2-aminoethyl)phenyl]-3-(2,4-dichlorophenyl)-3,4-dihydro-7-(phenylamino)- (9CI) (CA INDEX NAME)



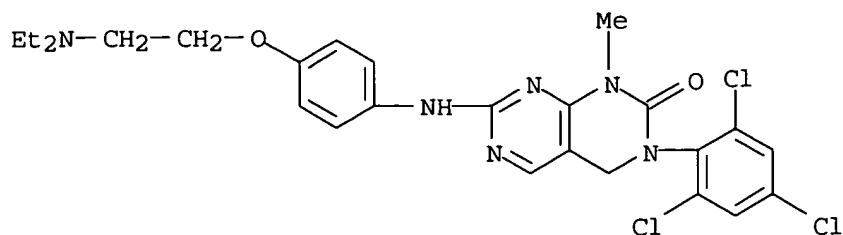
RN 266313-65-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,4-dichlorophenyl)-3,4-dihydro-1-[4-(hydroxymethyl)phenyl]-7-(phenylamino)- (9CI) (CA INDEX NAME)



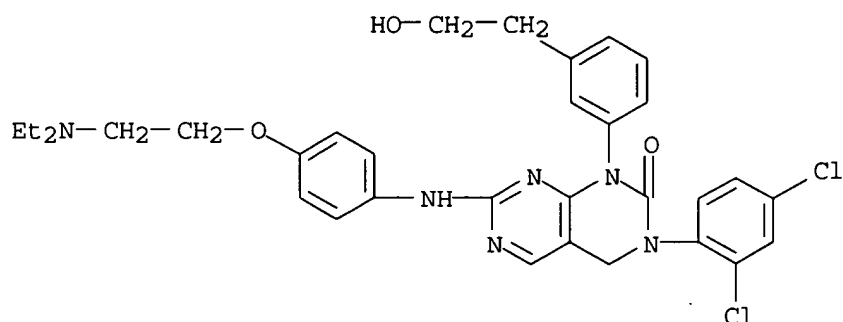
RN 266313-66-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-methyl-3-(2,4,6-trichlorophenyl)- (9CI) (CA INDEX NAME)



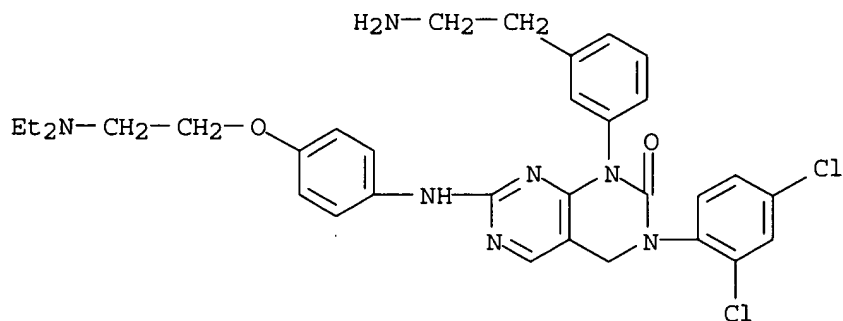
RN 266313-67-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,4-dichlorophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-[3-(2-hydroxyethyl)phenyl]- (9CI) (CA INDEX NAME)



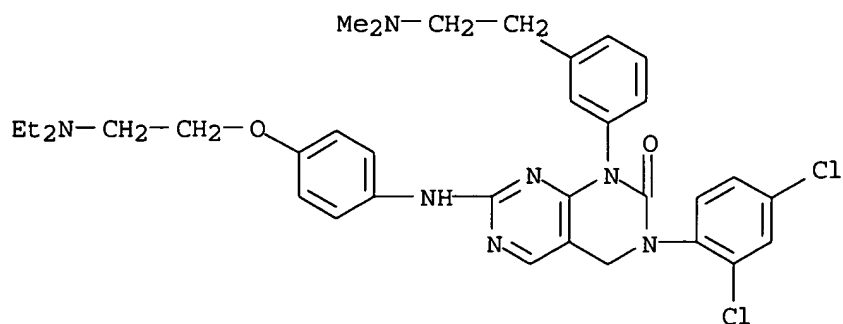
RN 266313-68-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[3-(2-aminoethyl)phenyl]-3-(2,4-dichlorophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro- (9CI) (CA INDEX NAME)



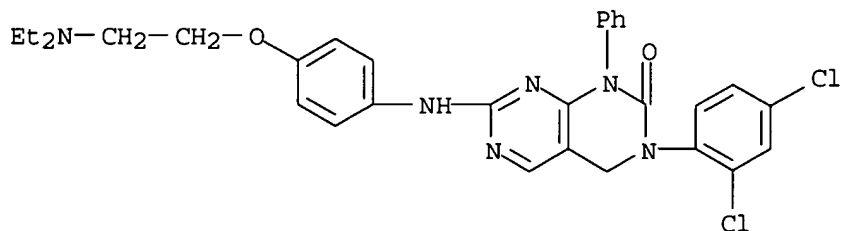
RN 266313-69-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,4-dichlorophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-1-[3-[2-(dimethylamino)ethyl]phenyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



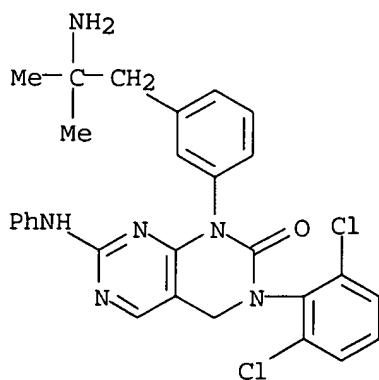
RN 266313-70-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,4-dichlorophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-phenyl- (9CI) (CA INDEX NAME)



RN 266313-71-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[3-(2-amino-2-methylpropyl)phenyl]-3-(2,6-dichlorophenyl)-3,4-dihydro-7-(phenylamino)- (9CI) (CA INDEX NAME)



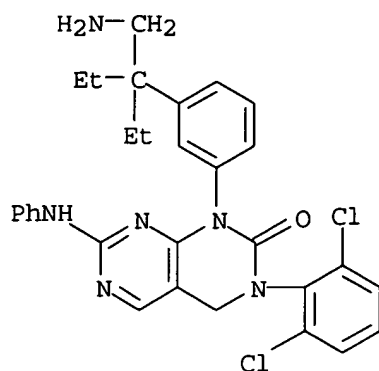
RN 266313-73-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[3-[1-(aminomethyl)-1-ethylpropyl]phenyl]-3-(2,6-dichlorophenyl)-3,4-dihydro-7-(phenylamino)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 266313-72-8

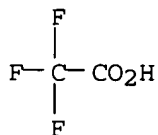
CMF C30 H30 Cl2 N6 O



CM 2

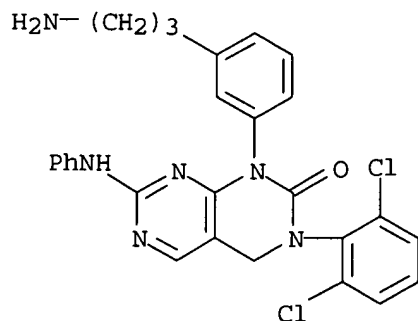
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CMF C2 H F3 O2



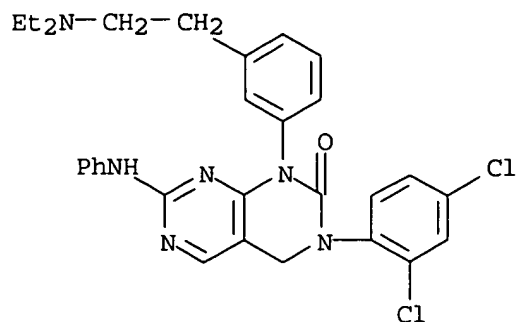
RN 266313-74-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-[3-(3-aminopropyl)phenyl]-3-(2,6-dichlorophenyl)-3,4-dihydro-7-(phenylamino)- (9CI) (CA INDEX NAME)



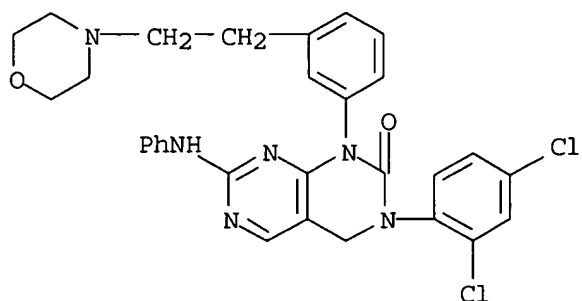
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CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,4-dichlorophenyl)-1-[3-[2-(diethylamino)ethyl]phenyl]-7-(phenylamino)- (9CI) (CA INDEX NAME)



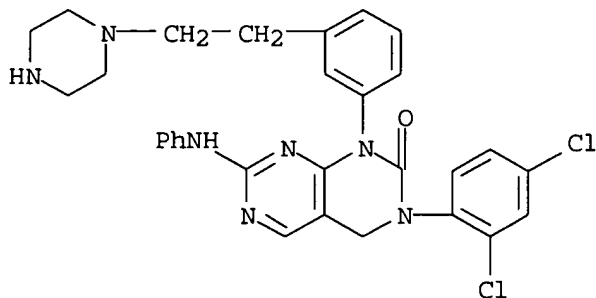
RN 266313-76-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,4-dichlorophenyl)-3,4-dihydro-1-[3-[2-(4-morpholinyl)ethyl]phenyl]-7-(phenylamino)- (9CI) (CA INDEX NAME)



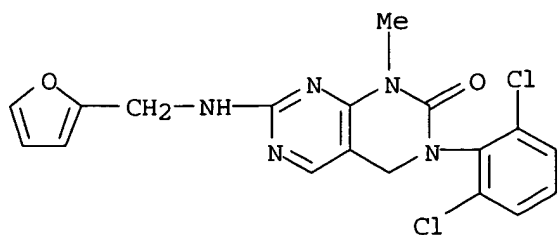
RN 266313-77-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,4-dichlorophenyl)-3,4-dihydro-7-(phenylamino)-1-[3-[2-(1-piperazinyl)ethyl]phenyl]- (9CI) (CA INDEX NAME)



RN 266313-78-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-7-[(2-furanylmethyl)amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



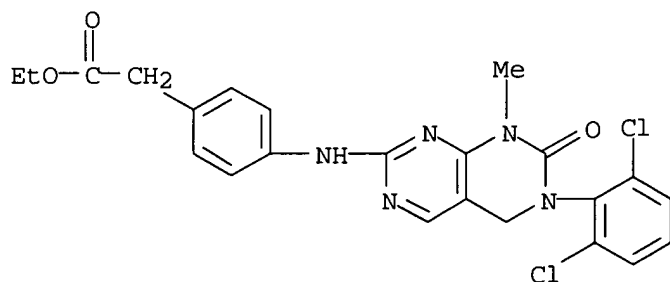
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 266314-91-4P 266314-92-5P 266314-93-6P
 266315-34-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(preparation of pyrimidopyrimidinones as T-cell tyrosine kinase inhibitors)

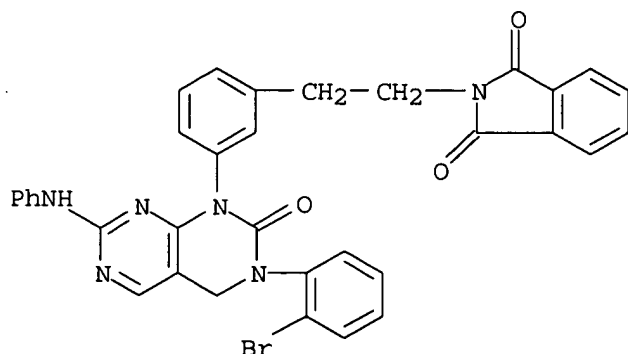
RN 266314-05-0 HCAPLUS

CN Benzeneacetic acid, 4-[[6-(2,6-dichlorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



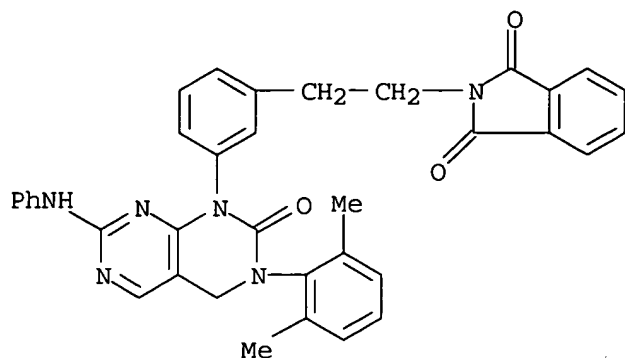
RN 266314-38-9 HCAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[3-[3-(2-bromophenyl)-3,4-dihydro-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]phenyl]ethyl]- (9CI) (CA INDEX NAME)



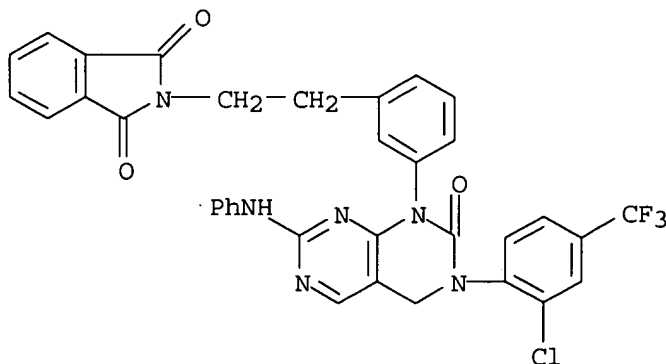
RN 266314-39-0 HCAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[3-[3-(2,6-dimethylphenyl)-3,4-dihydro-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]phenyl]ethyl]-(9CI)
(CA INDEX NAME)



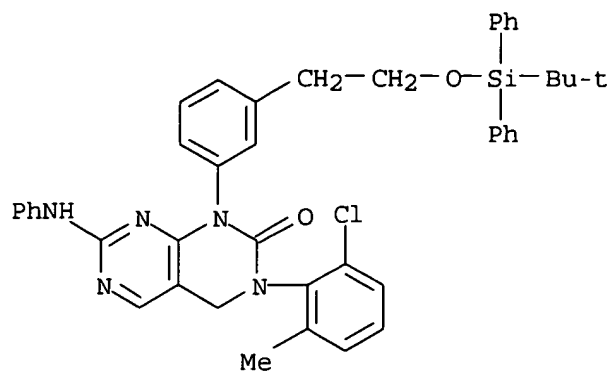
RN 266314-40-3 HCAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[3-[3-[2-chloro-4-(trifluoromethyl)phenyl]-3,4-dihydro-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]phenyl]ethyl]-(9CI) (CA INDEX NAME)



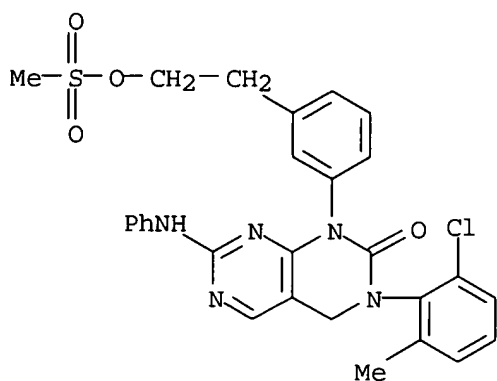
RN 266314-45-8 HCAPLUS

CN Pyrimido[4,5-b]pyrimidin-2(1H)-one, 3-(2-chloro-6-methylphenyl)-1-[3-[2-[[[1,1-dimethylethyl]diphenylsilyl]oxy]ethyl]phenyl]-3,4-dihydro-7-(phenylamino)-(9CI) (CA INDEX NAME)



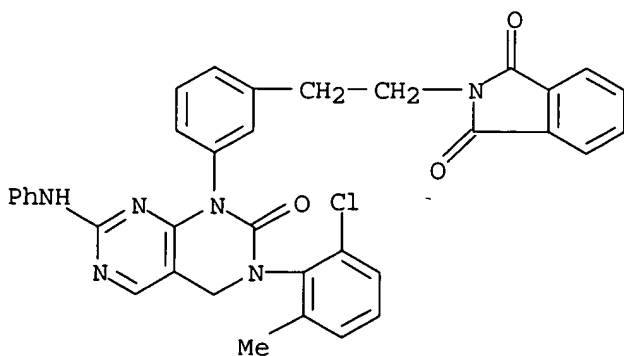
RN 266314-46-9 HCAPLUS

CN Pyrimido[4,5-b]pyrimidin-2(1H)-one, 3-(2-chloro-6-methylphenyl)-3,4-dihydro-1-[3-[2-[(methylsulfonyl)oxy]ethyl]phenyl]-7-(phenylamino)- (9CI)
(CA INDEX NAME)



RN 266314-47-0 HCAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[3-[3-(2-chloro-6-methylphenyl)-3,4-dihydro-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]phenyl]ethyl]- (9CI) (CA INDEX NAME)



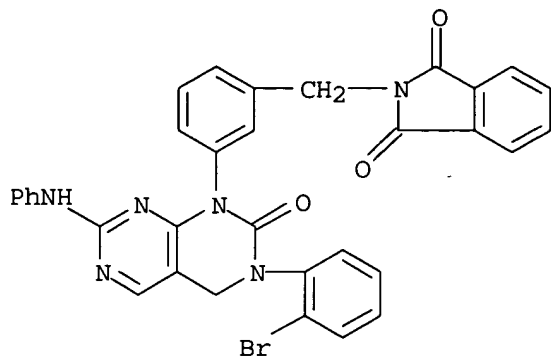
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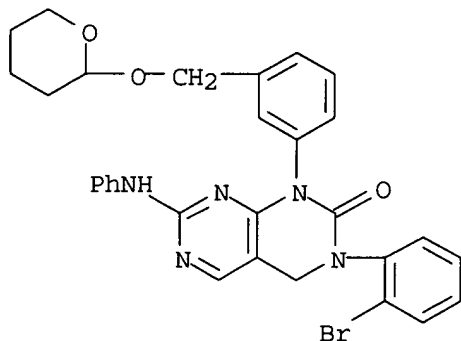
RN 266314-62-9 HCAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2-[[3-[3-(2-bromophenyl)-3,4-dihydro-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]phenyl]methyl]- (9CI) (CA INDEX NAME)



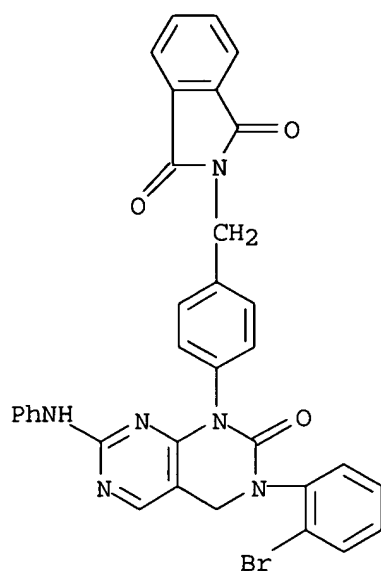
RN 266314-63-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-bromophenyl)-3,4-dihydro-7-(phenylamino)-1-[3-[[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)



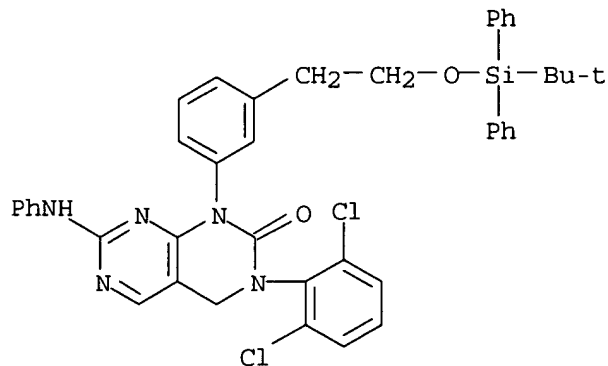
RN 266314-71-0 HCAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2-[[4-[3-(2-bromophenyl)-3,4-dihydro-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]phenyl]methyl]- (9CI) (CA INDEX NAME)



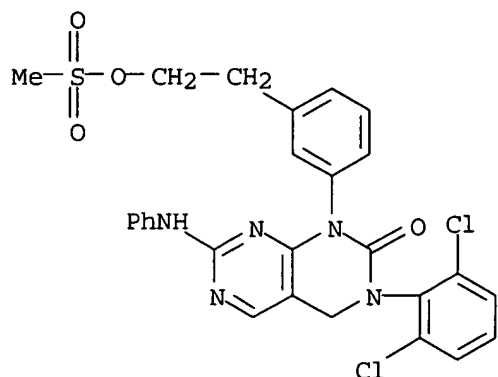
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CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-1-[3-[2-[(1,1-dimethylethyl)diphenylsilyl]oxy]ethyl]phenyl]-3,4-dihydro-7-(phenylamino)-(9CI) (CA INDEX NAME)



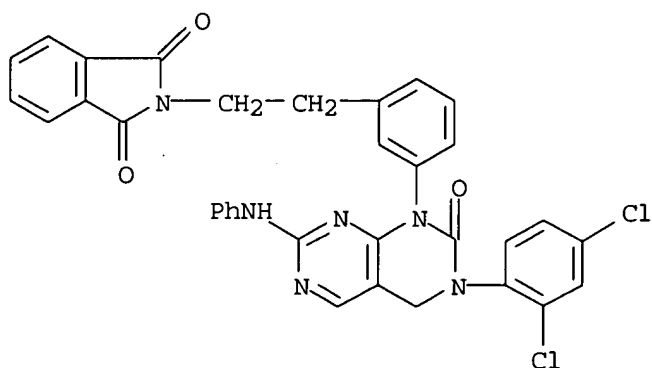
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CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-3,4-dihydro-1-[3-[2-[(methylsulfonyl)oxy]ethyl]phenyl]-7-(phenylamino)-(9CI) (CA INDEX NAME)



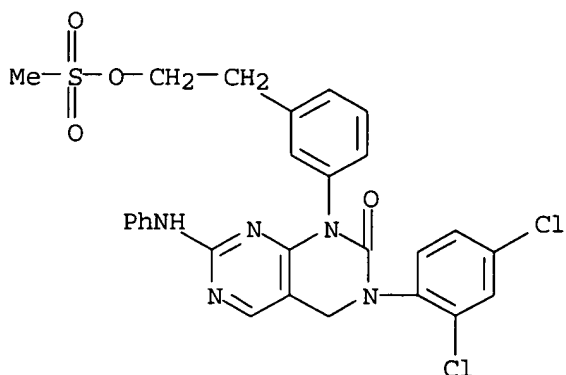
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CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[3-[3-(2,4-dichlorophenyl)-3,4-dihydro-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]phenyl]ethyl] - (9CI)
(CA INDEX NAME)



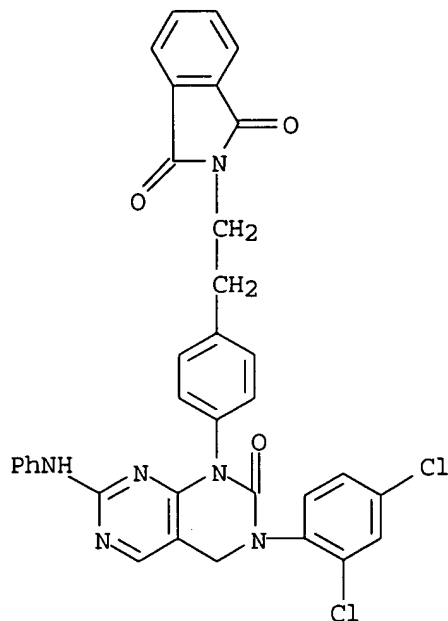
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CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,4-dichlorophenyl)-3,4-dihydro-1-[3-[2-[(methylsulfonyl)oxy]ethyl]phenyl]-7-(phenylamino) - (9CI) (CA INDEX NAME)

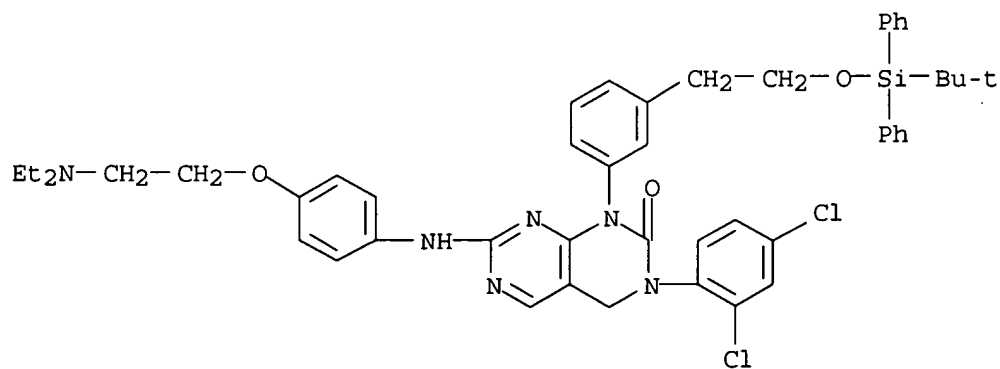


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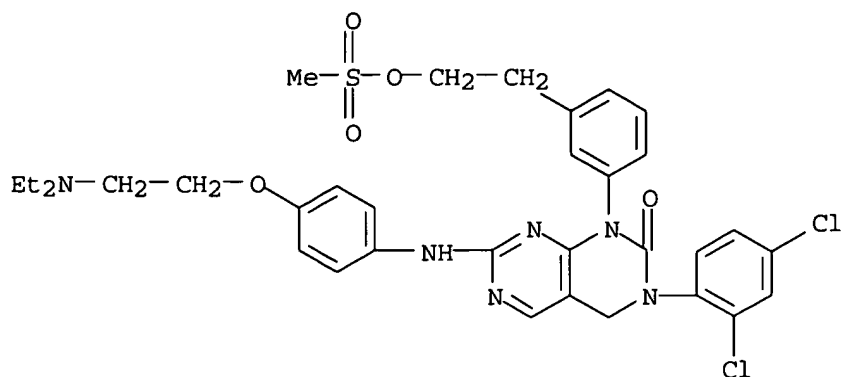
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-[3-(2,4-dichlorophenyl)-3,4-dihydro-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]phenyl]ethyl]- (9CI)
(CA INDEX NAME)



RN 266314-91-4 HCAPLUS
CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,4-dichlorophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-1-[3-[2-[[1,1-dimethylethyl)diphenylsilyl]oxy]ethyl]phenyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

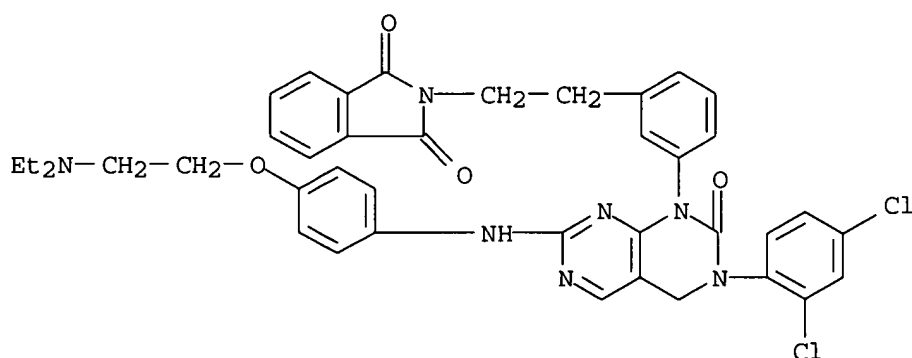


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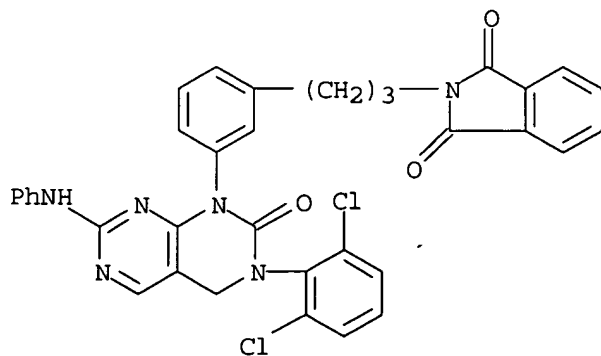
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CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[3-[3-(2,4-dichlorophenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3,4-dihydro-2-oxopyrimido[4,5-d]pyrimidin-1(2H)-yl]phenyl]ethyl]- (9CI) (CA INDEX NAME)



RN 266315-34-8 HCAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2-[3-[3-[3-(2,6-dichlorophenyl)-3,4-dihydro-2-oxo-7-(phenylamino)pyrimido[4,5-d]pyrimidin-1(2H)-yl]phenyl]propyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:764041 HCAPLUS

DOCUMENT NUMBER: 132:22971

TITLE: Preparation of oxopyrido- and -pyrimidopyrimidines as cellular proliferation inhibitors

INVENTOR(S): Dobrusin, Ellen Myra; Hamby, James Marino; Kramer, James Bernard; Schroeder, Mel Conrad; Showalter, Howard Daniel Hollis; Toogood, Peter; Trumpp-Kallmeyer, Susanne A.

PATENT ASSIGNEE(S): Warner-Lambert Co., USA

SOURCE: PCT Int. Appl., 133 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

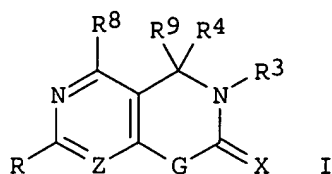
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PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|-------------|
| WO 9961444 | A2 | 19991202 | WO 1999-US10187 | 19990510 |
| WO 9961444 | A3 | 20000203 | | |
| W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
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| AU 9940734 | A1 | 19991213 | AU 1999-40734 | 19990510 |
| AU 763839 | B2 | 20030731 | | |
| BR 9911590 | A | 20010213 | BR 1999-11590 | 19990510 |
| EP 1080092 | A2 | 20010307 | EP 1999-924165 | 19990510 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| TR 200003429 | T2 | 20010723 | TR 2000-200003429 | 19990510 |
| JP 2002516327 | T2 | 20020604 | JP 2000-550849 | 19990510 |
| EE 200000706 | A | 20020617 | EE 2000-706 | 19990510 |
| NZ 508268 | A | 20040227 | NZ 1999-508268 | 19990510 |
| ZA 2000006536 | A | 20020211 | ZA 2000-6536 | 20001110 |
| BG 104960 | A | 20011031 | BG 2000-104960 | 20001117 |
| HR 2000000799 | A1 | 20010630 | HR 2000-799 | 20001120 |
| NO 2000005928 | A | 20001123 | NO 2000-5928 | 20001123 |
| HK 1039483 | A1 | 20040618 | HK 2001-107828 | 20011108 |
| US 2004044012 | A1 | 20040304 | US 2003-638848 | 20030811 |
| PRIORITY APPLN. INFO.: | | | US 1998-86708P | P 19980526 |
| | | | US 1999-126158P | P 19990325 |
| | | | WO 1999-US10187 | W 19990510 |
| | | | US 2000-623737 | A3 20000907 |

OTHER SOURCE(S): MARPAT 132:22971

GI



AB Title compds. [I; G = NR₂ or CHR₂; R = NHR₁ or SOO-2R₁; R₁,R₂ = H, (cyclo)alkyl, (un)substituted PH, -pyridyl, etc.; R₃ = groups cited for R₁, OH, alkoxy(carbonyl), etc.; R₄ = H; R₃R₄ = bond; R₈,R₉ = H, halo, NH₂, alkoxy-carbonyl, etc.; X = O, S, (alkyl)imino, etc.; Z =N or CH] were prepared as cyclin-dependant and tyrosine kinase inhibitors. Thus, 5-aminomethyl-4-cyclopentylamino-2-methylthiopyrimidine (preparation given) was cyclocondensed with 1,1'-carbonyldiimidazole and the oxidized product aminated by 4-(MeO)C₆H₄NH₂ to give I [G = cyclopentylimino, R = 4-(MeO)C₆H₄NH, R₃ = R₄ = R₈ = R₉ = H, X = O]. Data for biol. activity of I were given.

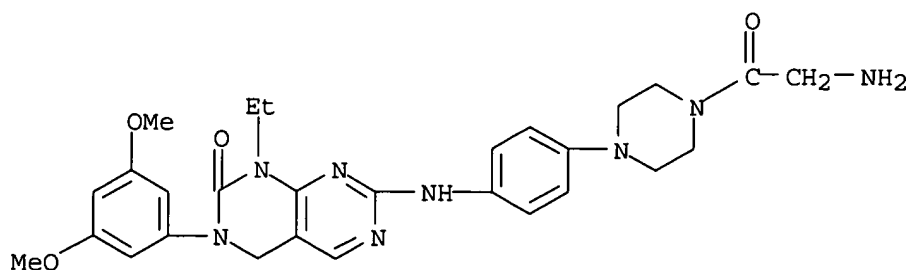
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 251371-93-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of bicyclic pyrimidines and bicyclic 3,4-dihydropyrimidines as inhibitors of cellular proliferation)

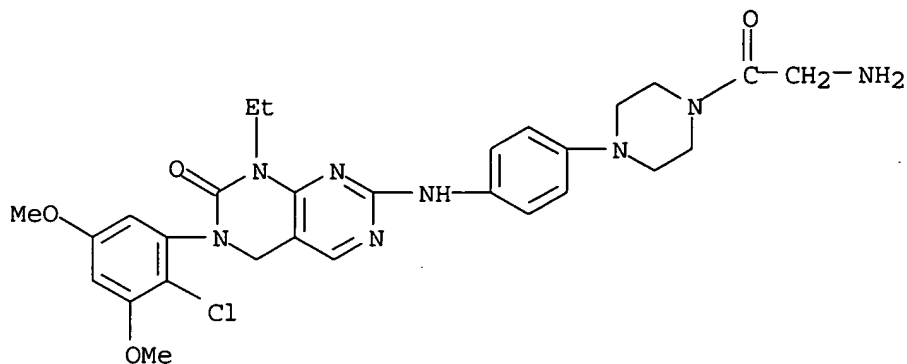
RN 251370-13-5 HCAPLUS

CN Piperazine, 1-(aminoacetyl)-4-[4-[6-(3,5-dimethoxyphenyl)-8-ethyl-5,6,7,8-tetrahydro-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]phenyl]- (9CI) (CA INDEX NAME)



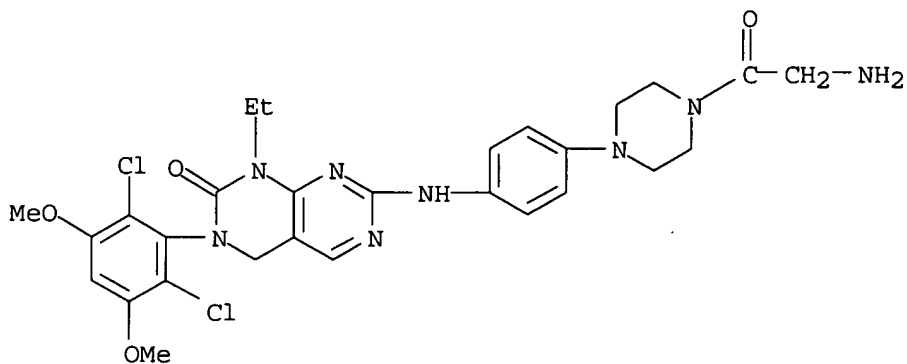
RN 251370-14-6 HCAPLUS

CN Piperazine, 1-(aminoacetyl)-4-[4-[[6-(2-chloro-3,5-dimethoxyphenyl)-8-ethyl-5,6,7,8-tetrahydro-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]phenyl]-(9CI) (CA INDEX NAME)



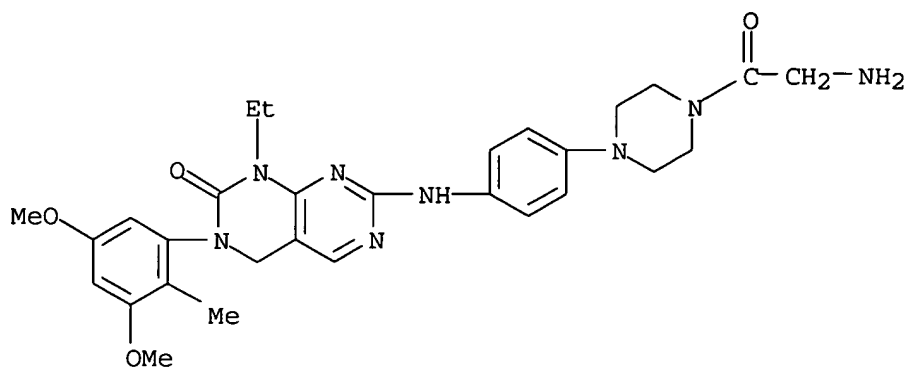
RN 251370-15-7 HCAPLUS

CN Piperazine, 1-(aminoacetyl)-4-[4-[[6-(2,6-dichloro-3,5-dimethoxyphenyl)-8-ethyl-5,6,7,8-tetrahydro-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]phenyl]-(9CI) (CA INDEX NAME)



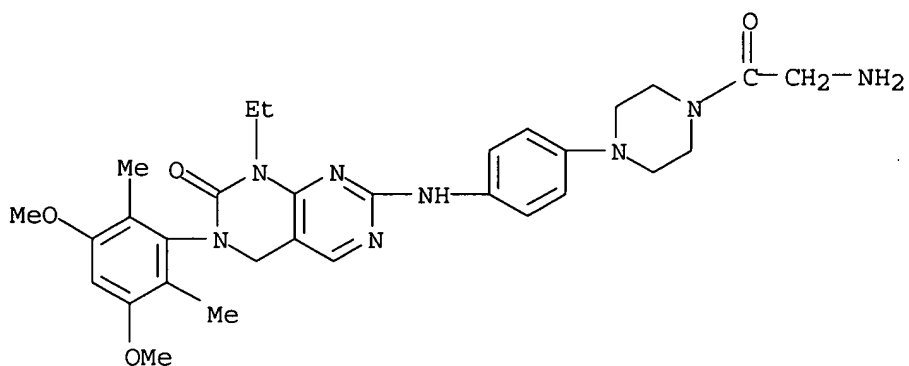
RN 251370-16-8 HCAPLUS

CN Piperazine, 1-(aminoacetyl)-4-[4-[[6-(3,5-dimethoxy-2-methylphenyl)-8-ethyl-5,6,7,8-tetrahydro-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]phenyl]-(9CI) (CA INDEX NAME)



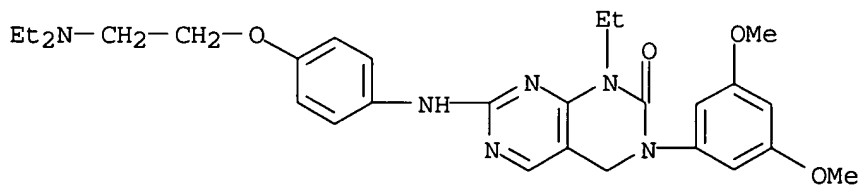
RN 251370-17-9 HCAPLUS

CN Piperazine, 1-(aminoacetyl)-4-[4-[[6-(3,5-dimethoxy-2,6-dimethylphenyl)-8-ethyl-5,6,7,8-tetrahydro-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]phenyl]-(9CI) (CA INDEX NAME)



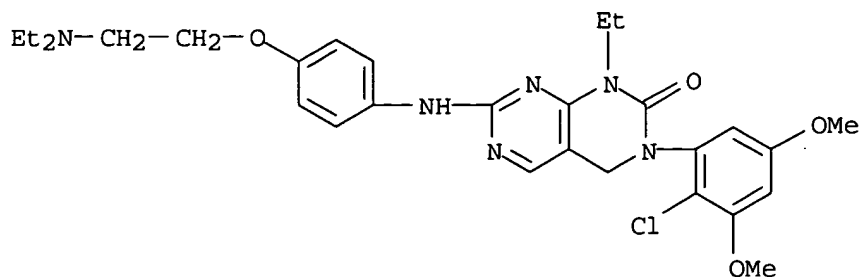
RN 251370-18-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3-(3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



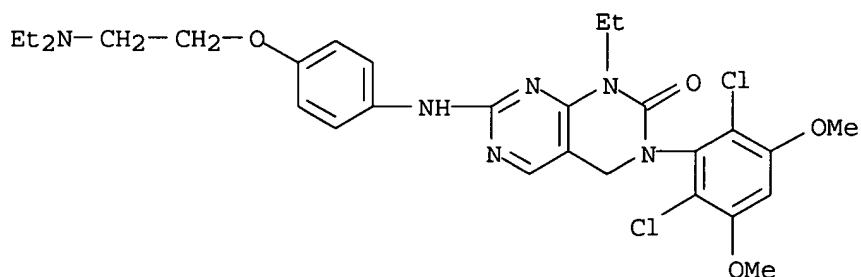
RN 251370-19-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chloro-3,5-dimethoxyphenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



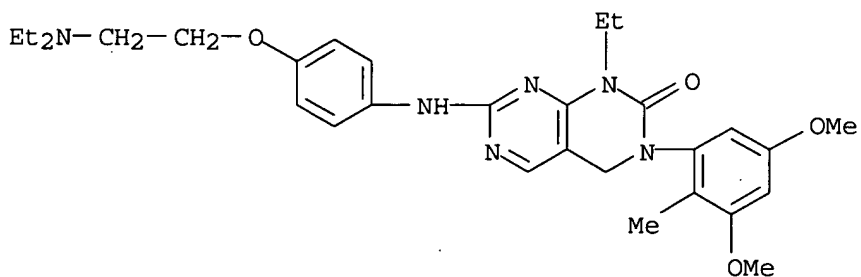
RN 251370-20-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichloro-3,5-dimethoxyphenyl)-7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



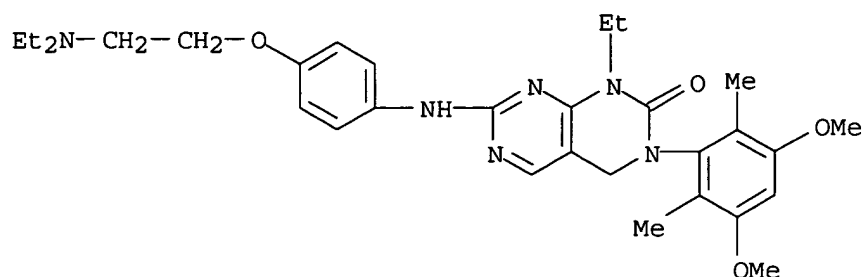
RN 251370-21-5 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3-(3,5-dimethoxy-2-methylphenyl)-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



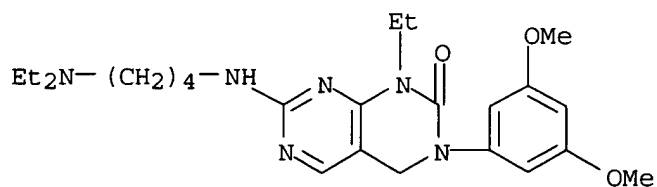
RN 251370-22-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3-(3,5-dimethoxy-2,6-dimethylphenyl)-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



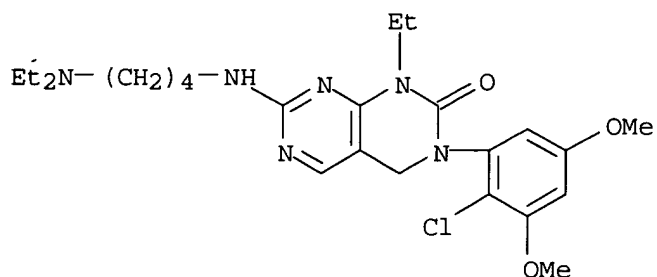
RN 251370-23-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[4-(diethylamino)butyl]amino]-3-(3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



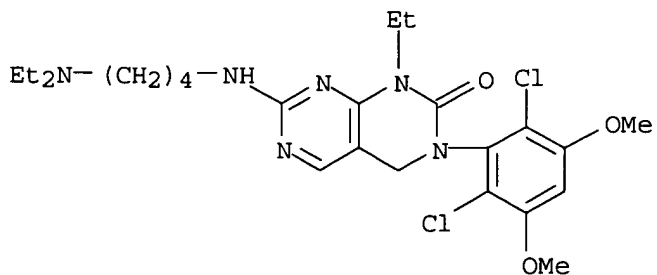
RN 251370-24-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chloro-3,5-dimethoxyphenyl)-7-[[4-(diethylamino)butyl]amino]-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



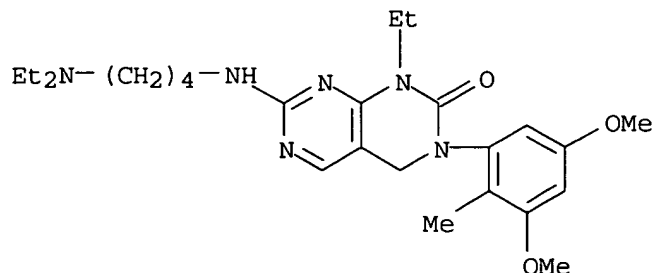
RN 251370-25-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichloro-3,5-dimethoxyphenyl)-7-[[4-(diethylamino)butyl]amino]-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



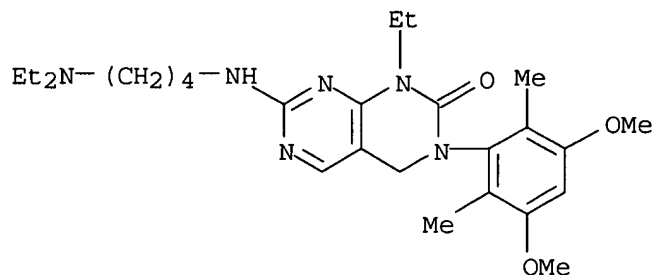
RN 251370-26-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[4-(diethylamino)butyl]amino]-3-(3,5-dimethoxy-2-methylphenyl)-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



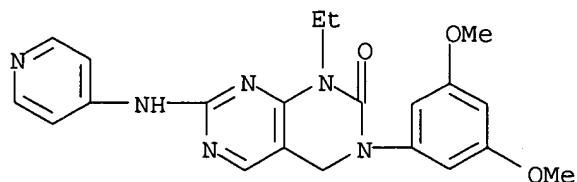
RN 251370-27-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[4-(diethylamino)butyl]amino]-3-(3,5-dimethoxy-2,6-dimethylphenyl)-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



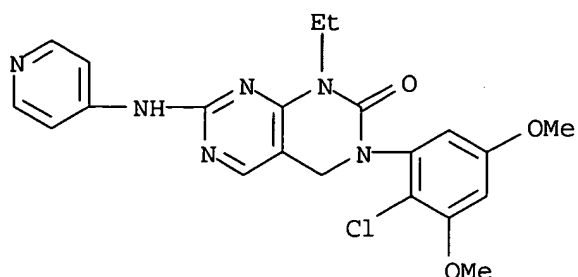
RN 251370-28-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro-7-(4-pyridinylamino)- (9CI) (CA INDEX NAME)



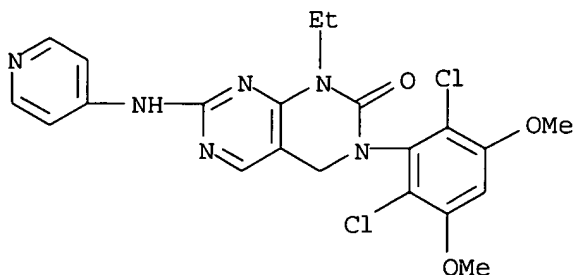
RN 251370-29-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2-chloro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro-7-(4-pyridinylamino)- (9CI) (CA INDEX NAME)



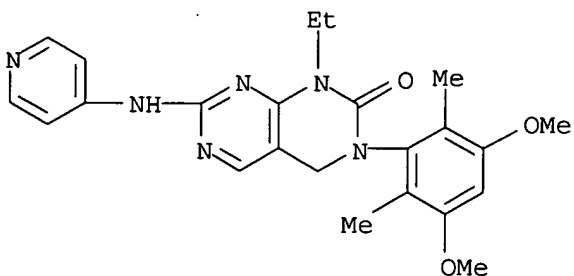
RN 251370-30-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichloro-3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro-7-(4-pyridinylamino)- (9CI) (CA INDEX NAME)



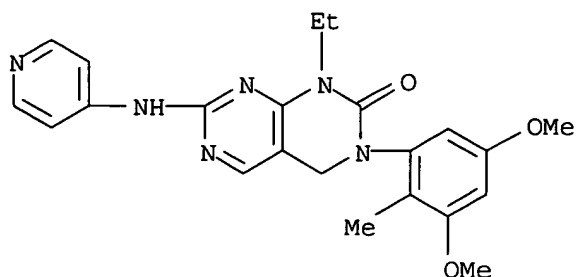
RN 251370-31-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(3,5-dimethoxy-2,6-dimethylphenyl)-1-ethyl-3,4-dihydro-7-(4-pyridinylamino)- (9CI) (CA INDEX NAME)



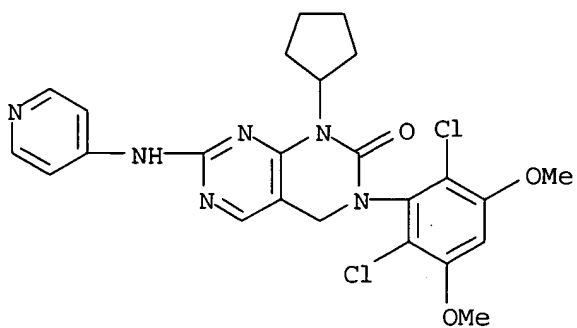
RN 251370-32-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(3,5-dimethoxy-2-methylphenyl)-1-ethyl-3,4-dihydro-7-(4-pyridinylamino)- (9CI) (CA INDEX NAME)



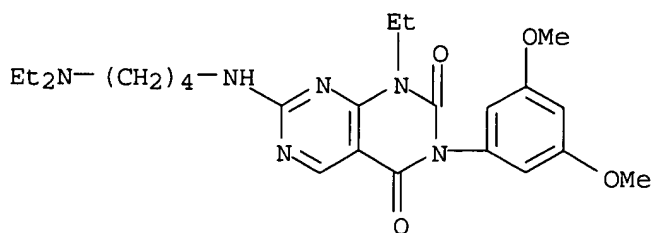
RN 251370-33-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 1-cyclopentyl-3-(2,6-dichloro-3,5-dimethoxyphenyl)-3,4-dihydro-7-(4-pyridinylamino)- (9CI) (CA INDEX NAME)



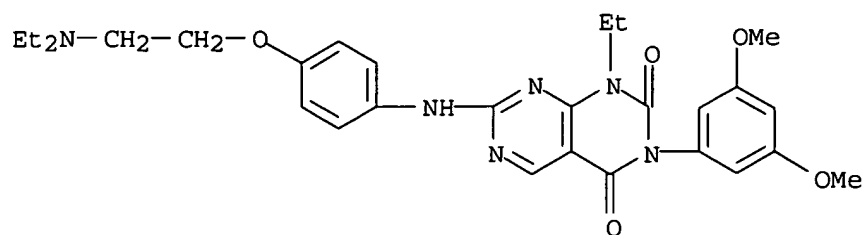
RN 251370-66-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-2,4(1H,3H)-dione, 7-[[4-(diethylamino)butyl]amino]-3-(3,5-dimethoxyphenyl)-1-ethyl- (9CI) (CA INDEX NAME)



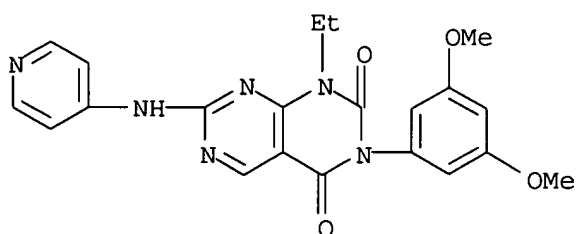
RN 251370-67-9 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-2,4(1H,3H)-dione, 7-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-3-(3,5-dimethoxyphenyl)-1-ethyl- (9CI) (CA INDEX NAME)



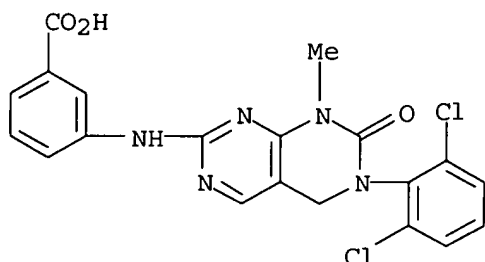
RN 251370-68-0 HCAPLUS

CN Pyrimido[4,5-d]pyrimidine-2,4(1H,3H)-dione, 3-(3,5-dimethoxyphenyl)-1-ethyl-7-(4-pyridinylamino)- (9CI) (CA INDEX NAME)



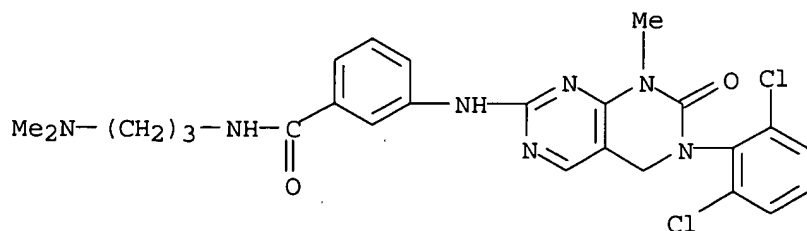
RN 251371-07-0 HCAPLUS

CN Benzoic acid, 3-[[6-(2,6-dichlorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]- (9CI) (CA INDEX NAME)



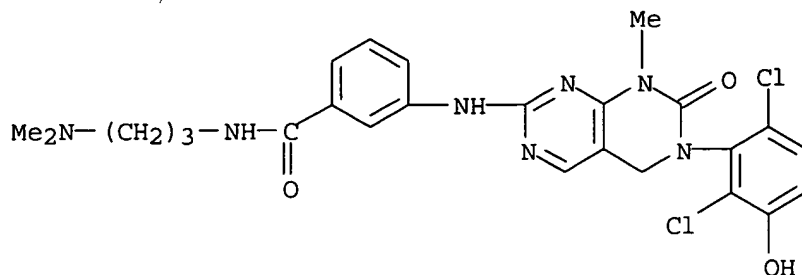
RN 251371-08-1 HCAPLUS

CN Benzamide, 3-[[[6-(2,6-dichlorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-N-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



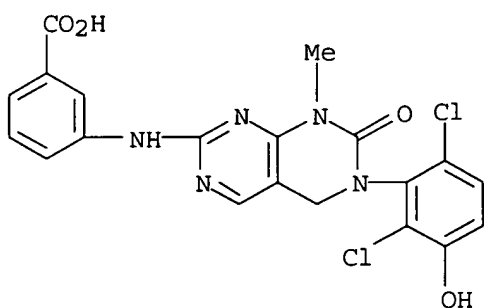
RN 251371-09-2 HCAPLUS

CN Benamide, 3-[[6-(2,6-dichloro-3-hydroxyphenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]-N-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



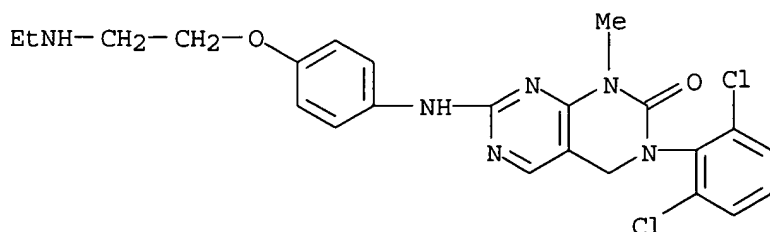
RN 251371-10-5 HCAPLUS

CN Benzoic acid, 3-[[6-(2,6-dichloro-3-hydroxyphenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]- (9CI) (CA INDEX NAME)



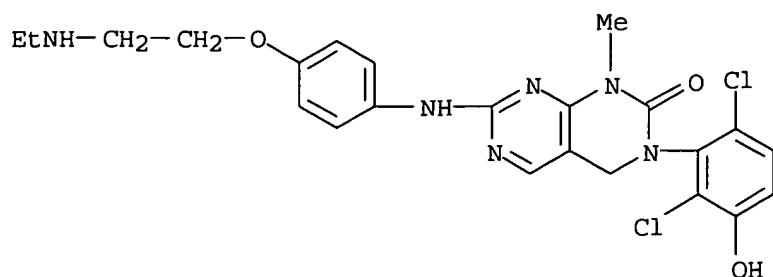
RN 251371-11-6 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichlorophenyl)-7-[[4-[2-(ethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



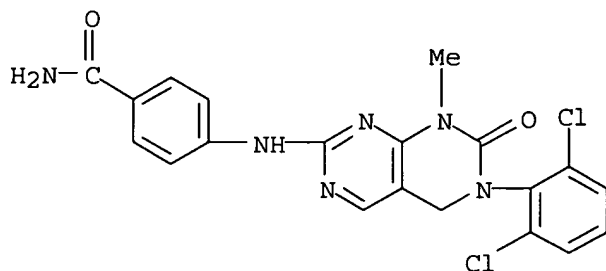
RN 251371-12-7 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichloro-3-hydroxyphenyl)-7-[[4-[2-(ethylamino)ethoxy]phenyl]amino]-3,4-dihydro-1-methyl- (9CI) (CA INDEX NAME)



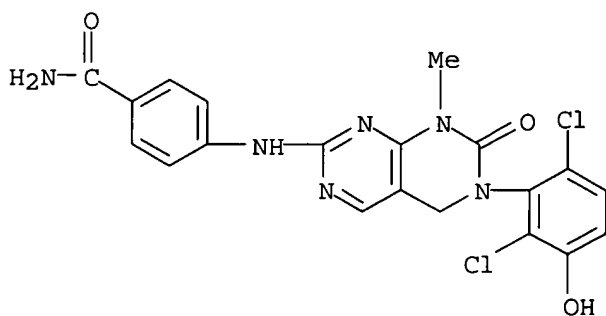
RN 251371-13-8 HCAPLUS

CN Benzamide, 4-[[6-(2,6-dichlorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]- (9CI) (CA INDEX NAME)



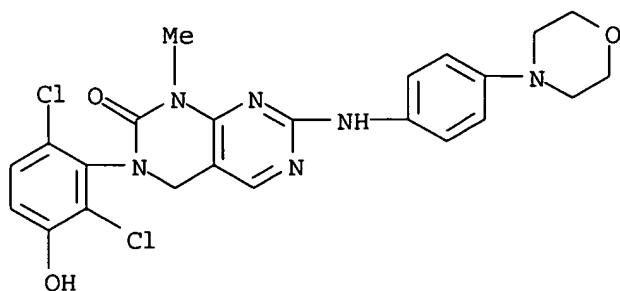
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CN Benzamide, 4-[[6-(2,6-dichloro-3-hydroxyphenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]- (9CI) (CA INDEX NAME)



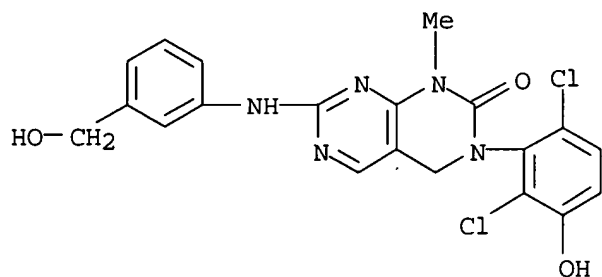
RN 251371-17-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichloro-3-hydroxyphenyl)-3,4-dihydro-1-methyl-7-[[4-(4-morpholinyl)phenyl]amino]- (9CI) (CA INDEX NAME)



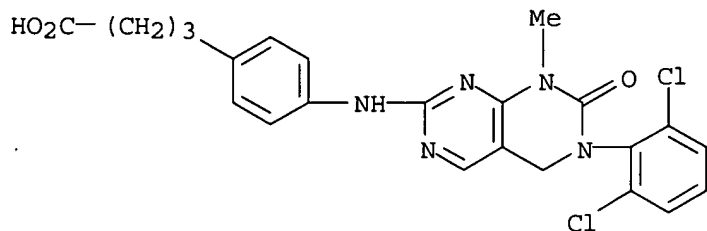
RN 251371-18-3 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(2,6-dichloro-3-hydroxyphenyl)-3,4-dihydro-7-[[3-(hydroxymethyl)phenyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



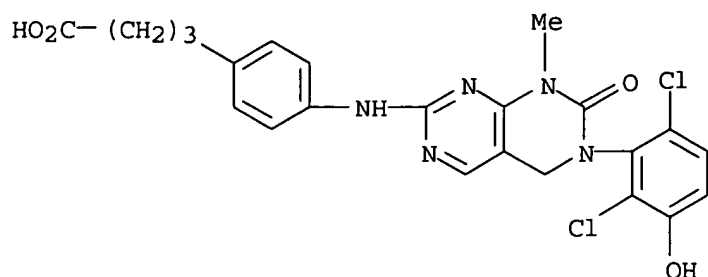
RN 251371-19-4 HCAPLUS

CN Benzenebutanoic acid, 4-[[6-(2,6-dichlorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]- (9CI) (CA INDEX NAME)



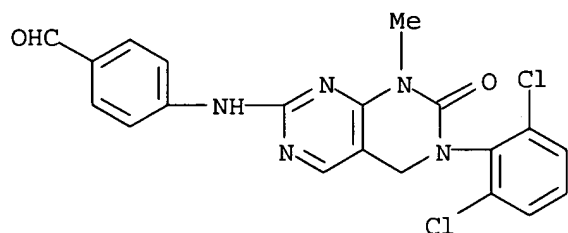
RN 251371-20-7 HCAPLUS

CN Benzenebutanoic acid, 4-[[6-(2,6-dichloro-3-hydroxyphenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino]- (9CI) (CA INDEX NAME)



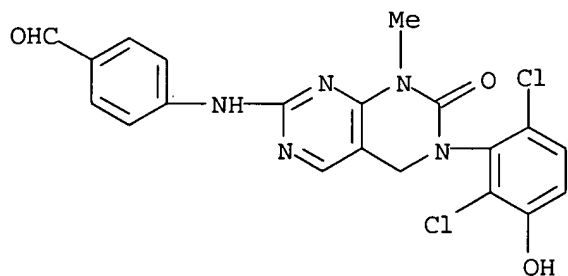
RN 251371-21-8 HCAPLUS

CN Benzaldehyde, 4-[[[6-(2,6-dichlorophenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino] - (9CI) (CA INDEX NAME)



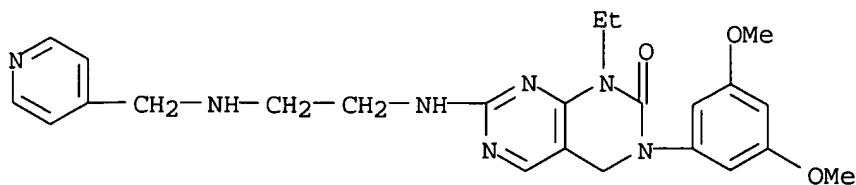
RN 251371-22-9 HCAPLUS

CN Benzaldehyde, 4-[[[6-(2,6-dichloro-3-hydroxyphenyl)-5,6,7,8-tetrahydro-8-methyl-7-oxopyrimido[4,5-d]pyrimidin-2-yl]amino] - (9CI) (CA INDEX NAME)



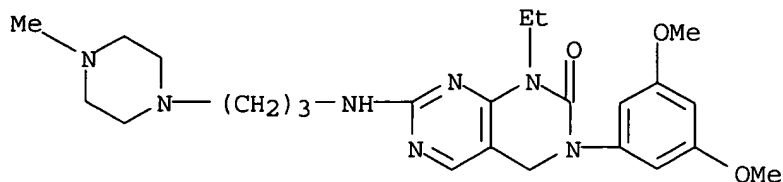
RN 251371-89-8 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro-7-[[2-[(4-pyridinylmethyl)amino]ethyl]amino] - (9CI) (CA INDEX NAME)



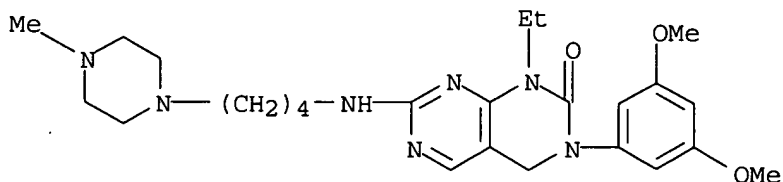
RN 251371-90-1 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro-7-[[3-(4-methyl-1-piperazinyl)propyl]amino] - (9CI) (CA INDEX NAME)



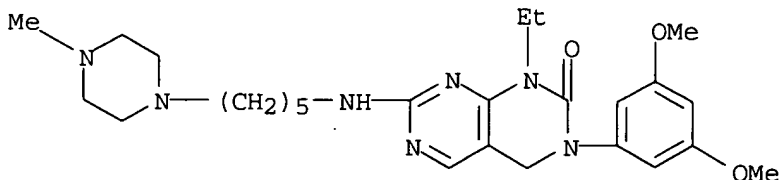
RN 251371-91-2 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro-7-[[4-(4-methyl-1-piperazinyl)butyl]amino] - (9CI) (CA INDEX NAME)



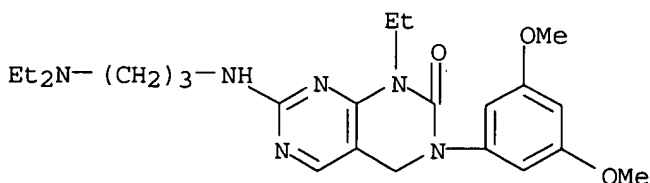
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CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 3-(3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro-7-[[5-(4-methyl-1-piperazinyl)pentyl]amino] - (9CI) (CA INDEX NAME)

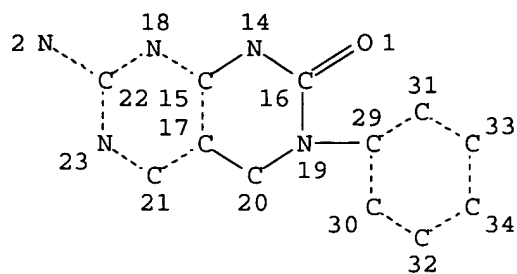


RN 251371-93-4 HCAPLUS

CN Pyrimido[4,5-d]pyrimidin-2(1H)-one, 7-[[3-(diethylamino)propyl]amino]-3-(3,5-dimethoxyphenyl)-1-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



=> d que stat 127
L24 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
L26 790 SEA FILE=REGISTRY SSS FUL L24
L27 12 SEA FILE=HCAPLUS ABB=ON L26

=> d his ful

FILE 'REGISTRY' ENTERED AT 15:19:43 ON 14 MAY 2005

L24 STRUCTURE 651734-33-7

L25 32 SEA SSS SAM L24

L26 790 SEA SSS FUL L24

*) see d que stat for structure
790 compda in Reg.
12 cit's in CA Plus*

FILE 'HCAPLUS' ENTERED AT 15:21:02 ON 14 MAY 2005

L27 12 SEA ABB=ON L26